******* QUERY RESULTS *******
(EXAMPLE # 57)

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=> d ide l12

L12  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   676633-18-4  REGISTRY
ED   Entered STN:  26 Apr 2004
CN   L-Valinamide, N,O,β,β-tetramethyl-L-tyrosyl-N-[(1S,2E)-3-
     carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI)  (CA INDEX
     NAME)
FS   STEREOSEARCH
MF   C28 H45 N3 O5
CI   COM
SR   CA
LC   STN Files:   CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.
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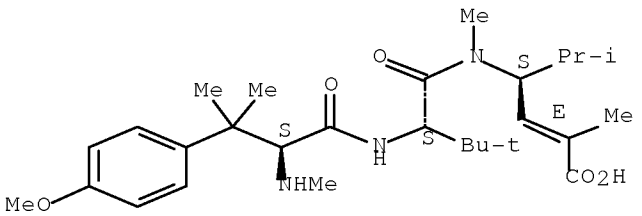


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d his l13

     (FILE 'STNGUIDE' ENTERED AT 13:52:43 ON 09 MAR 2009)

     FILE 'HCAPLUS' ENTERED AT 13:56:34 ON 09 MAR 2009
L13           1 S L12

=> d que l13
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L8             6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND VALINAMIDE
L9             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND TYROSYL
L10            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND CARBOXY
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  676633-18-4/RN
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 OR L11
L13            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12


=> d l13 ibib abs hitstr hitind


L13  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2004:267231  HCAPLUS  Full-text
DOCUMENT NUMBER:          140:304081
TITLE:                    Preparation of peptides for treating resistant tumors
INVENTOR(S):              Greenberger, Lee Martin; Loganzo, Frank, Jr.;
                          Discafani-Marro, Carolyn Mary; Zask, Arie;
                          Ayral-Kaloustian, Semiramis
PATENT ASSIGNEE(S):       Wyeth Holdings Corporation, USA
SOURCE:                   PCT Int. Appl., 442 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2004026293        A2    20040401    WO 2003-US29832        20030918
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             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2406504           A1    20040320    CA 2002-2406504        20021003
     AU 2003275126        A1    20040408    AU 2003-275126         20030918
     US 20040121965       A1    20040624    US 2003-666722         20030918
PRIORITY APPLN. INFO.:                      US 2002-411883P     P  20020920
                                            WO 2003-US29832     W  20030918

OTHER SOURCE(S):          MARPAT 140:304081
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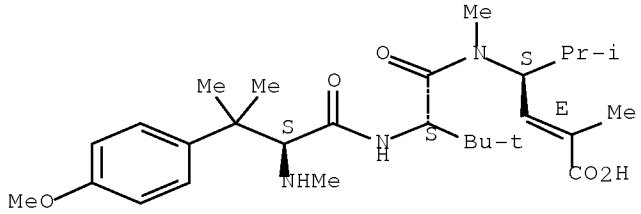
AB The invention provides peptides R1R2NCH(CR3R4R5)CONR6CHR7CONR8R9 [R1-R8 are H or an (un)saturated moiety having a linear, branched, or cyclic skeleton containing 1-10 (un)substituted carbon atoms and 0-4 each nitrogen, oxygen, or sulfur atoms; or R1R2N or R3R4C is a 3- to 7-membered ring; R9 is -Y-CO-Z, where Y is alkyl and Z is OH, SH, NH2, an amino acid residue, etc. (with provisos)] for treating or inhibiting the growth or eradication of tumors which are resistant to at least one chemotherapeutic agent. Thus, N,β,β-trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and shown to be a potent inhibitor of cell growth in 34 tumor cell lines (mean IC50 = 2.1 ± 1.7 nM, median 1.7 nM, range 0.2-7.3 nM) and is distinct from paclitaxel which has an usually large range of activity. The activity is independent of tumor origin and in many cases this peptide is considerably more potent than paclitaxel.

IT 676633-18-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating resistant tumors)
RN 676633-18-4 HCAPLUS
CN L-Valinamide, N,O,β,β-tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating resistant tumors)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

******* QUERY RESULTS *******
(COMPOUNDS FROM CLAIMS 28-51 AND OVARIAN CANCERS)

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=> d his l74

     (FILE 'HCAPLUS' ENTERED AT 16:29:04 ON 09 MAR 2009)
L74           1 S L73 AND (L41 OR L42)

=> d que l74
L41       24618 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "OVARY, NEOPLASM"/CT
L42       35118 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (OVARIAN OR OVARY OR OVARIES)
                (S) (CANCER? OR TUMOR? OR TUMOUR? OR NEOPLAS? OR CARCIN?)
L51        2185 SEA FILE=REGISTRY ABB=ON  PLU=ON  3(L)(DIMETHYL?) (L) VALINAMID
                E
L52       16609 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 (L) ((HEXENO? OR HEXEONATE
                OR HEP(W)ENOIC) (W) ACID)
L53          46 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) VALINAMIDE
L54           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) ALLOTHREONINAMID
                E
L57          92 SEA FILE=REGISTRY ABB=ON  PLU=ON  (DIMETHYL OR METHYL) (2W)
                LEUCINAMIDE
L59           7 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL (2W) ISOLEUCINAMIDE
L61           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  DIMETHYL (2W) HEXENAMIDE
L62          91 SEA FILE=REGISTRY ABB=ON  PLU=ON  PHENYL? (2W) PENTENOI?
L63           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) NORVALINAMIDE
L64           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRIMETHYL? (2W) HEXENAMID?
L67       19034 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L51 OR L52 OR L53 OR L54)
                OR L57 OR L59 OR L61 OR L62 OR (L63 OR L64)
L70             STR
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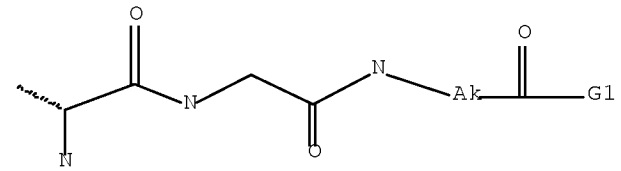
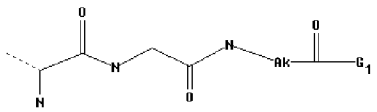
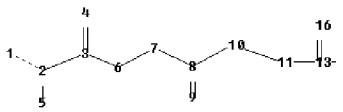


G1 O,S,N

Structure attributes must be viewed using STN Express query preparation:

Uploading L4.str





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ring/chain nodes :
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chain bonds :
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exact/norm bonds :
1-2  2-5  3-4  3-6  6-7  8-9  8-10  10-11  11-13  13-15  13-16
exact bonds :
2-3  7-8


G1:O,S,N

Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  13:CLASS  15:CLASS  16:CLASS
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L72         395 SEA FILE=REGISTRY SUB=L67 SSS FUL L70
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L74           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND (L41 OR L42)


=> d l74 1 ibib abs hitstr hitind

L74  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2005:346897  HCAPLUS  Full-text
DOCUMENT NUMBER:         142:404292
TITLE:                   Compositions and methods for increasing drug
                         efficiency
INVENTOR(S):             Ballatore, Carlo; Castellino, Angelo John; Desharnais,
                         Joel; Guo, Zijan; Li, Quing; Newman, Michael James;
                         Sun, Chengzao
PATENT ASSIGNEE(S):      Dihedron Corporation, USA
SOURCE:                  PCT Int. Appl., 404 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

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     WO 2005035003        A2    20050421    WO 2004-US31148        20040922
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     WO 2005035003        A9    20070823
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

US 20050148534	A1	20050707	US 2004-948364		20040922
US 20050187147	A1	20050825	US 2004-948707		20040922
US 20060234909	A1	20061019	US 2006-376695		20060314
PRIORITY APPLN. INFO.:			US 2003-505325P	P	20030922
			US 2004-568340P	P	20040504
			US 2004-581835P	P	20040622
			US 2003-505033P	P	20030922
			US 2004-948707	B1	20040922

OTHER SOURCE(S): MARPAT 142:404292

AB In one embodiment, provided herein are compns. and methods for increasing drug efficiency. In certain embodiments, the compns. contain conjugates having the formula: D-L-S wherein D is a drug moiety; L, which may or may not be present, is a non-releasing linker moiety; and S is a substrate for a protein or lipid kinase that is overexpressed, overactive or exhibits undesired activity in a target system.

IT 850498-42-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

RN 850498-42-9 HCAPLUS

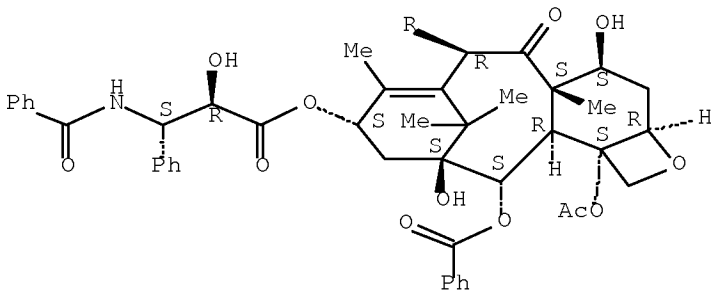
CN L-Valinamide, N2-(2,2-dimethyl-1-oxopropyl)-L-arginyl-L-leucyl-L-valyl-L-alanyl-L-tyrosyl-L-α-glutamylglycyl-L-tyrosyl-N-[15-[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl]oxy]-15-oxo-4,7,10-trioxa-14-azapentadec-1-yl]-, phenylmethyl ester, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 850498-41-8
CMF C118 H159 N15 O31

Absolute stereochemistry.

PAGE 1-A



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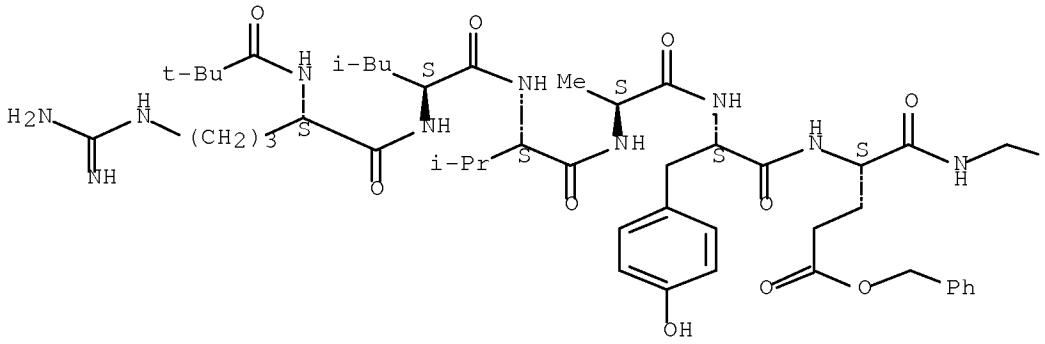

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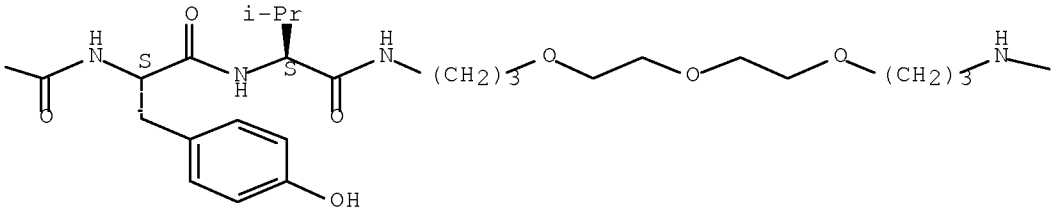
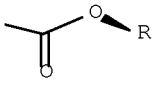


PAGE 2-C



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CRN 76-05-1
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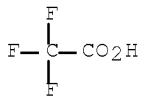


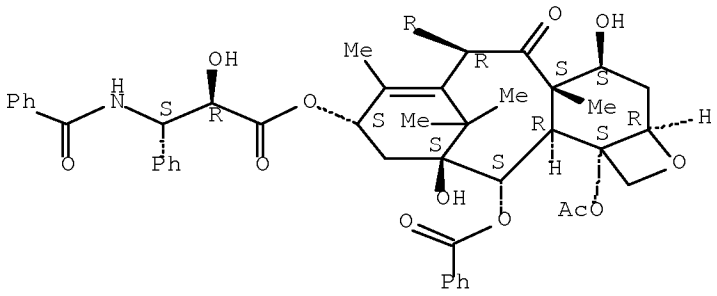
IT 850498-41-8 850499-32-0 850499-34-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

RN 850498-41-8 HCAPLUS

CN L-Valinamide, N2-(2,2-dimethyl-1-oxopropyl)-L-arginyl-L-leucyl-L-valyl-L-alanyl-L-tyrosyl-L-α-glutamylglycyl-L-tyrosyl-N-[15-[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl]oxy]-15-oxo-4,7,10-trioxa-14-azapentadec-1-yl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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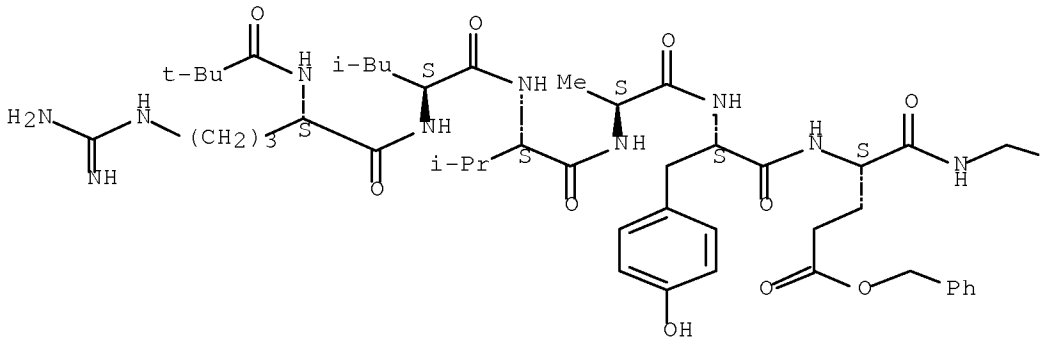
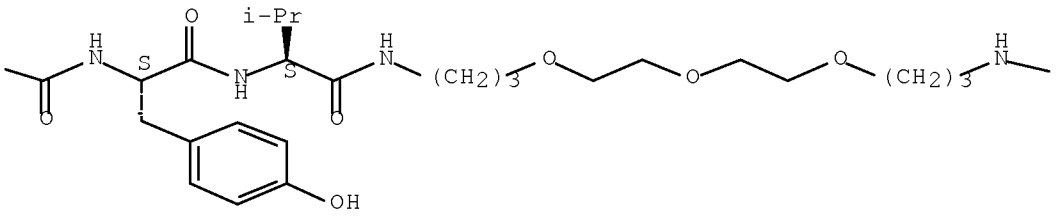


PAGE 2-B



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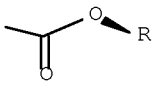
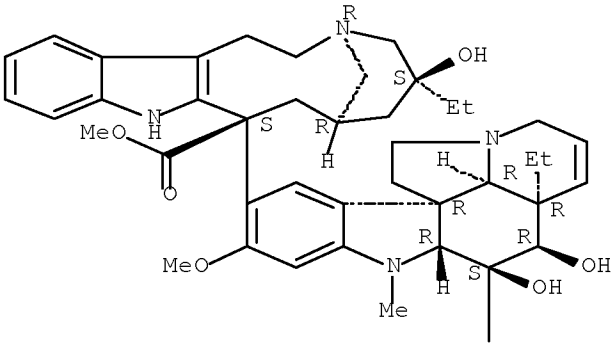


RN 850499-32-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, amide with N2-(2,2-dimethyl-1-oxopropyl)-L-arginyl-L-leucyl-L-valyl-L-alanyl-L-tyrosyl-L-α-glutamylglycyl-L-tyrosyl-N-[2-[2-[2-(2-aminoethoxy)ethoxy]ethoxy]ethyl]-L-valinamide [4-[[1-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3-methylbutyl]amino]phenyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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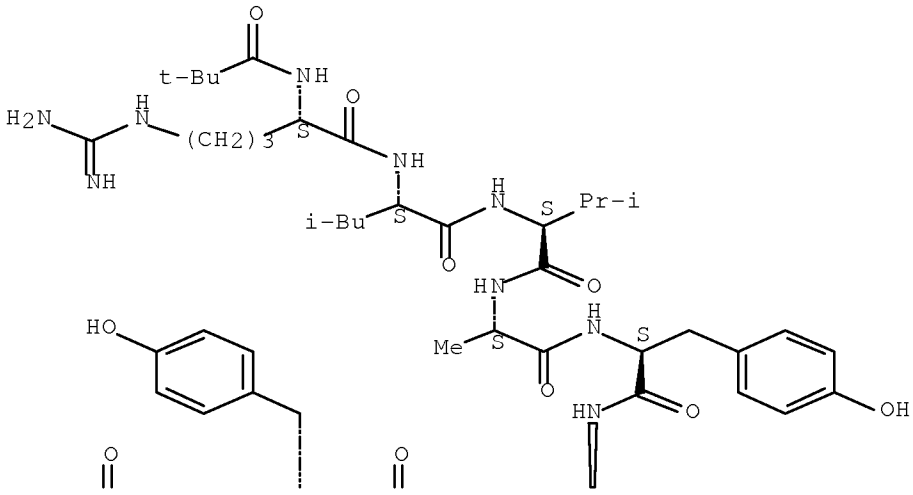

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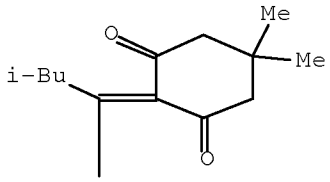

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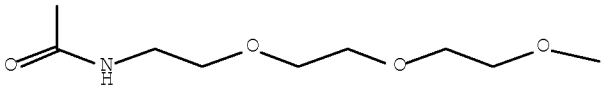

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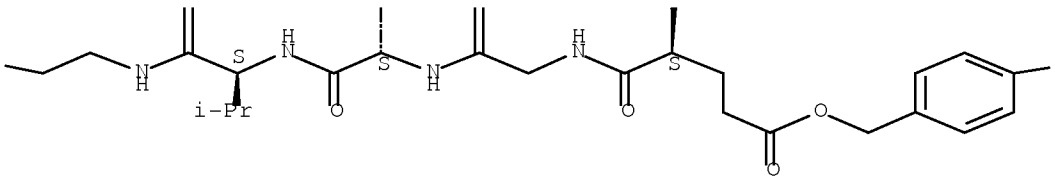

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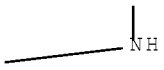

RN 850499-34-2 HCAPLUS
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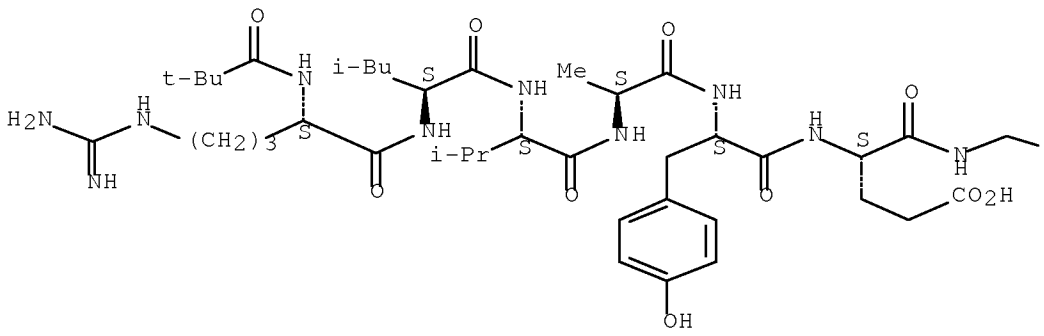
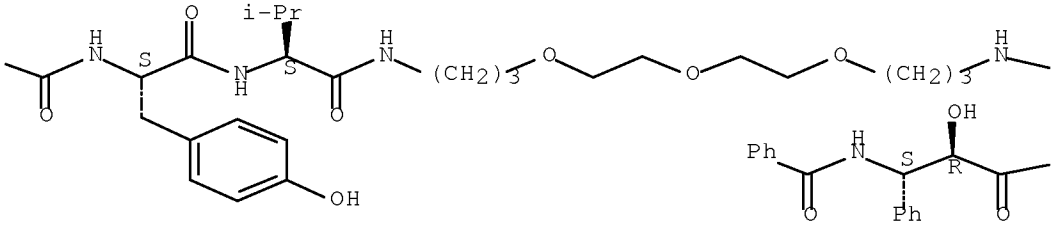
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl]oxy]-15-oxo-4,7,10-trioxa-14-azapentadec-1-yl]- (9CI) (CA INDEX NAME)

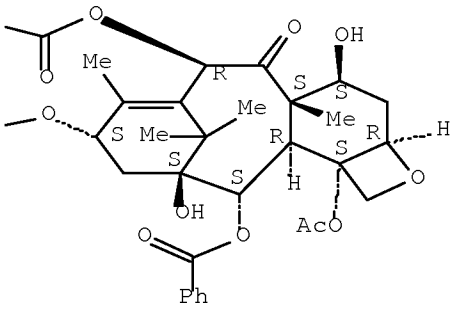
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





IC ICM A61K047-48
ICS C07K007-06; A61K038-08; A61P029-00; A61P035-00; A61K031-337; A61K031-475; A61K031-704

CC 1-12 (Pharmacology)
Section cross-reference(s): 34, 63

IT Acute lymphocytic leukemia
Angiogenesis
Asthma
Autoimmune disease
Bladder, neoplasm
Brain, neoplasm
Chronic lymphocytic leukemia
Chronic myeloid leukemia
Connective tissue, disease
Drug delivery systems
Esophagus, neoplasm
Hairy cell leukemia
Head and Neck, neoplasm
Head and Neck, neoplasm
Hodgkin's disease
Kidney, neoplasm
Leukemia
Liver, neoplasm
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Mouth, neoplasm
Multiple myeloma
Multiple sclerosis
Neoplasm
Neuroglia, neoplasm
Osteoporosis
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Psoriasis
Rheumatoid arthritis
Sarcoma
Skin, neoplasm
Testis, neoplasm

Transplant rejection
(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

IT 850498-06-5P 850498-08-7P 850498-10-1P 850498-12-3P 850498-14-5P
850498-16-7P 850498-18-9P 850498-20-3P 850498-22-5P 850498-23-6P
850498-24-7P 850498-25-8P 850498-26-9P 850498-28-1P 850498-29-2P
850498-31-6P 850498-32-7P 850498-34-9P 850498-36-1P 850498-38-3P
850498-40-7P 850498-42-9P 850498-44-1P 850498-46-3P
850498-48-5P 850498-50-9P 850498-52-1P 850498-54-3P 850498-56-5P
850498-58-7P 850498-60-1P 850498-62-3P 850498-64-5P 850498-66-7P
850498-68-9P 850498-70-3P 850498-72-5P 850498-74-7P 850498-75-8P
850498-77-0P 850498-79-2P 850498-81-6P 850498-83-8P 850498-85-0P
850498-87-2P 850498-89-4P 850498-91-8P 850498-93-0P 850498-95-2P
850498-97-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

IT 50-07-7D, Mitomycin C, conjugates 50-18-0D, Cyclophosphamide, conjugates
50-44-2D, 6-Mercaptopurine, conjugates 51-21-8D, 5-Fluorouracil, conjugates 54-62-6D, Aminopterin, conjugates 57-22-7D, Vincristine, conjugates 59-05-2D, Methotrexate, conjugates 91-18-9D, Pteridine, derivs., conjugates 147-94-4D, Cytosine arabinoside, conjugates 148-82-3D, Melphalan, conjugates 518-28-5D, Podophyllotoxin, derivs., conjugates 528-74-5D, Dichloromethotrexate, conjugates 801-52-5D, Porfiromycin, conjugates 865-21-4, Vinblastine 1404-00-8D, Mitomycin, derivs., conjugates 2410-93-7D, Methopterin, conjugates 2998-57-4D, Estramustine, conjugates 3352-69-0D, 4-Desacetylvinblastine, conjugates 11056-06-7D, Bleomycin, derivs., conjugates 15228-71-4D, Leurosidine, conjugates 15663-27-1D, Cisplatin, conjugates 20830-81-3D, Daunorubicin, conjugates 23214-92-8D, Doxorubicin, derivs. 33069-62-4D, Paclitaxel, derivs. 33419-42-0D, Etoposide, conjugates 50935-04-1D, conjugates 53643-48-4D, Vindesine, conjugates 57103-68-1D, Maytansinol, conjugates 78432-77-6, 10-Desacetyl taxol 82855-09-2D, Combretastatin, conjugates 111372-15-7 114977-28-5D, Docetaxel, conjugates 117091-64-2D, Etoposide phosphate, conjugates 146307-39-3 152044-53-6D, Epothilone A, conjugates 152044-54-7D, Epothilone B, conjugates 220167-86-2 849206-51-5 849206-90-2
849206-91-3 849206-92-4 849206-93-5 849206-94-6 850497-99-3
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850499-52-4 850499-53-5 850499-54-6 850499-55-7 850499-56-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

******* QUERY RESULTS *******
(COMPOUNDS FROM CLAIMS 28-51 AND CANCERS/NEOPLASMS)

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=> d his l76

     (FILE 'HCAPLUS' ENTERED AT 16:29:04 ON 09 MAR 2009)
L76          59 S L75 NOT L74

          FILE 'STNGUIDE' ENTERED AT 16:38:15 ON 09 MAR 2009

=> d que l76
L41       24618 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "OVARY, NEOPLASM"/CT
L42       35118 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (OVARIAN OR OVARY OR OVARIES)
                (S) (CANCER? OR TUMOR? OR TUMOUR? OR NEOPLAS? OR CARCIN?)
L51        2185 SEA FILE=REGISTRY ABB=ON  PLU=ON  3(L)(DIMETHYL?) (L) VALINAMID
                E
L52       16609 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 (L) ((HEXENO? OR HEXEONATE
                OR HEP(W)ENOIC) (W) ACID)
L53          46 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) VALINAMIDE
L54           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) ALLOTHREONINAMID
                E
L57          92 SEA FILE=REGISTRY ABB=ON  PLU=ON  (DIMETHYL OR METHYL) (2W)
                LEUCINAMIDE
L59           7 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL (2W) ISOLEUCINAMIDE
L61           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  DIMETHYL (2W) HEXENAMIDE
L62          91 SEA FILE=REGISTRY ABB=ON  PLU=ON  PHENYL? (2W) PENTENOI?
L63           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  METHYL? (2W) NORVALINAMIDE
L64           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRIMETHYL? (2W) HEXENAMID?
L67       19034 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L51 OR L52 OR L53 OR L54)
                OR L57 OR L59 OR L61 OR L62 OR (L63 OR L64)
L70           STR
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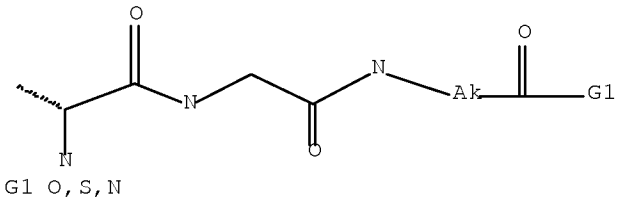

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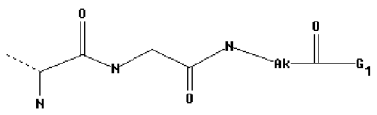
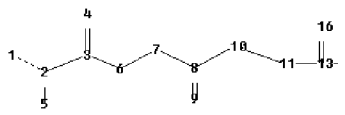
Uploading L4.str





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2  3  4  6  7  8  9  10  11  13  15  16
ring/chain nodes :
1  5
chain bonds :
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exact/norm bonds :
1-2  2-5  3-4  3-6  6-7  8-9  8-10  10-11  11-13  13-15  13-16
exact bonds :
2-3  7-8


G1:O,S,N

Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  13:CLASS  15:CLASS  16:CLASS
Element Count :
Node 11: Limited
    C,C1-6




L72          395 SEA FILE=REGISTRY SUB=L67 SSS FUL L70
L73          276 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND (L41 OR L42)
L75           60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND (CANCER? OR NEOPLAS?
                 OR TUMOR? OR TUMOUR? OR CARCIN?)
L76           59 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L74


=> d l76 1-59 ibib abs hitstr hitind

L76  ANSWER 1 OF 59  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2008:1137000  HCAPLUS  Full-text
DOCUMENT NUMBER:          149:448726
TITLE:                    Preparation of peptides comprising tryptophan-lysine
                          (arginine) fragments as anticancer agents
INVENTOR(S):              Wang, Dexin; Wang, Nan; Gong, Xi; Yan, Zheng; Han,
                          Xiang; Yang, Xiaoxiao; Feng, Hehe
PATENT ASSIGNEE(S):       Institute of Materia Medica, Chinese Academy of
                          Medical Sciences, Peop. Rep. China
SOURCE:                   Faming Zhuanli Shenqing Gongkai Shuomingshu, 15pp.
                          CODEN: CNXXEV
DOCUMENT TYPE:            Patent
LANGUAGE:                 Chinese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     CN 101265290          A     20080917    CN 2007-10064397        20070314
PRIORITY APPLN. INFO.:                       CN 2007-10064397        20070314
OTHER SOURCE(S):          MARPAT 149:448726
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AB The invention discloses the design and synthesis of peptides comprising tryptophan-lysine (arginine) fragments such as (Cys-Phe-D-Trp-Lys-Val)2Lys-NHMe and the method for preparing the peptides through liquid phase, solid phase or liquid-solid phase techniques. The peptides can be used for preparing anti-cancer medicine, especially for treating gastric cancer, cervical cancer, skin cancer, and breast cancer.

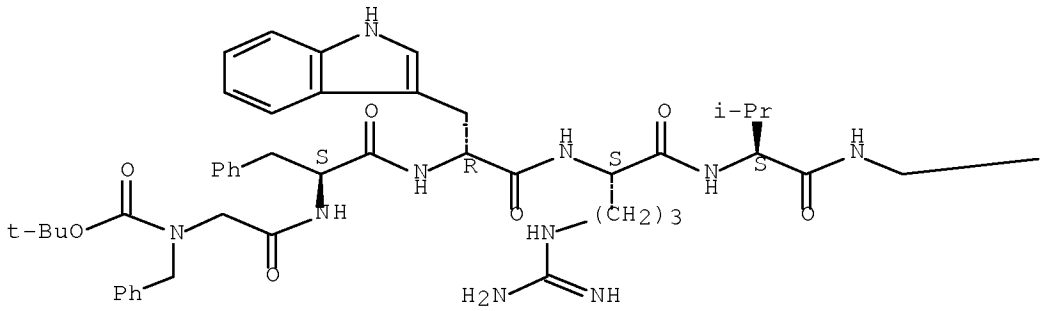
IT 1067920-32-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides comprising tryptophan-lysine (arginine) fragments as anticancer agents)

RN 1067920-32-4 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-N-(phenylmethyl)glycyl-L-phenylalanyl-D-tryptophyl-L-arginyl-N-(3-pyridinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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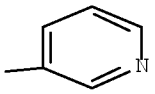


CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT Antitumor agents
Cervix, neoplasm
Mammary gland, neoplasm
Neoplasm
Skin, neoplasm
Stomach, neoplasm
(preparation of peptides comprising tryptophan-lysine (arginine) fragments as anticancer agents)

IT 1067920-03-9P 1067920-06-2P 1067920-16-4P 1067920-22-2P

1067920-32-4P 1067920-35-7P 1067920-38-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides comprising tryptophan-lysine (arginine) fragments as anticancer agents)

L76 ANSWER 2 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1136539 HCAPLUS Full-text
DOCUMENT NUMBER: 149:439660
TITLE: Novel Peptide Linkers for Highly Potent Antibody-Auristatin Conjugate
AUTHOR(S): Doronina, Svetlana O.; Bovee, Tim D.; Meyer, David W.; Miyamoto, Jamie B.; Anderson, Martha E.; Morris-Tilden, Carol A.; Senter, Peter D.
CORPORATE SOURCE: Seattle Genetics Incorporated, Bothell, WA, 98021, USA
SOURCE: Bioconjugate Chemistry (2008), 19(10), 1960-1963
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

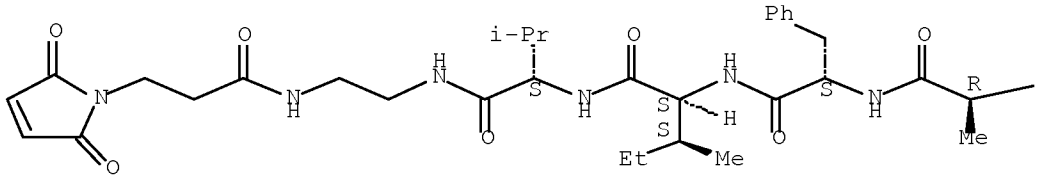
AB Auristatins are highly potent antimitotic agents that have received considerable attention because of their activities when targeted to tumor cells in the form of antibody-drug conjugates (ADCs). Our lead agent, SGN-35, consists of the cAC10 antibody linked to the N-terminal amino acid of monomethylauristatin E (MMAE) via a valine-citrulline p-aminobenzylcarbamate (val-cit-PABC) linker that is cleaved by intracellular proteases such as cathepsin B. More recently, we developed an auristatin F (AF) derivative monomethylauristatin F (MMAF), which unlike MMAE contains the amino acid phenylalanine at the C-terminal position. Because of the neg. charged C-terminal residue, the potency of AF and MMAF is impaired. However, their ability to kill target cells is greatly enhanced through facilitated cellular uptake by internalizing mAbs. Here, we explore the effects of linker technol. on AF-based ADC potency, activity, and tolerability by generating a diverse set of dipeptide linkers between the C-terminal residue and the mAb carrier. The resulting ADCs differed widely in activity, with some having significantly improved therapeutic indexes compared to the original mAb-Val-Cit-PABC-MMAF conjugate. The therapeutic index was increased yet further by generating dipeptide-based ADCs utilizing new auristatins with methionine or tryptophan as the C-terminal drug residue. These results demonstrate that manipulation of the C-terminal peptide sequence used to attach auristatins to the mAb carrier can lead to highly potent and specific conjugates with greatly improved therapeutic windows.

IT 1070273-51-6DP, reaction products with cysteine thiol of IF6 antibody 1070273-53-8DP, reaction products with cysteine thiol of IF6 antibody 1070273-55-0DP, reaction products with cysteine thiol of IF6 antibody
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide linkers for highly potent antibody-auristatin conjugate)

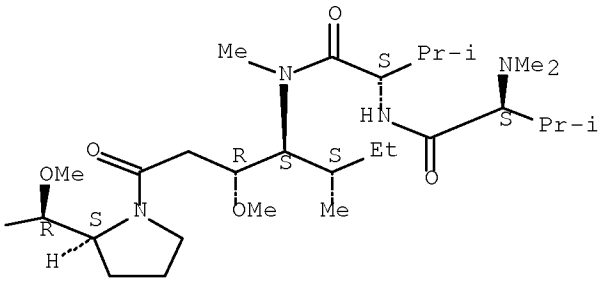
RN 1070273-51-6 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-isoleucyl-N-[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



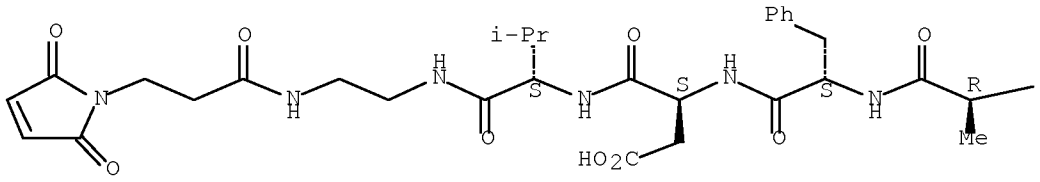
PAGE 1-B



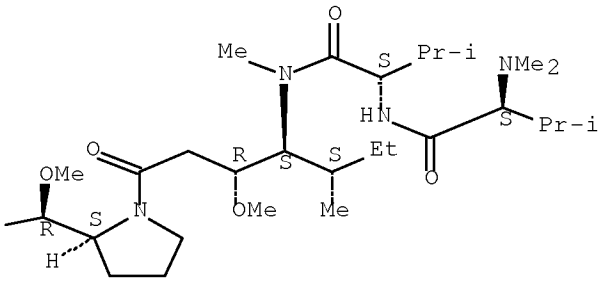
RN 1070273-53-8 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-α-aspartyl-N-[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



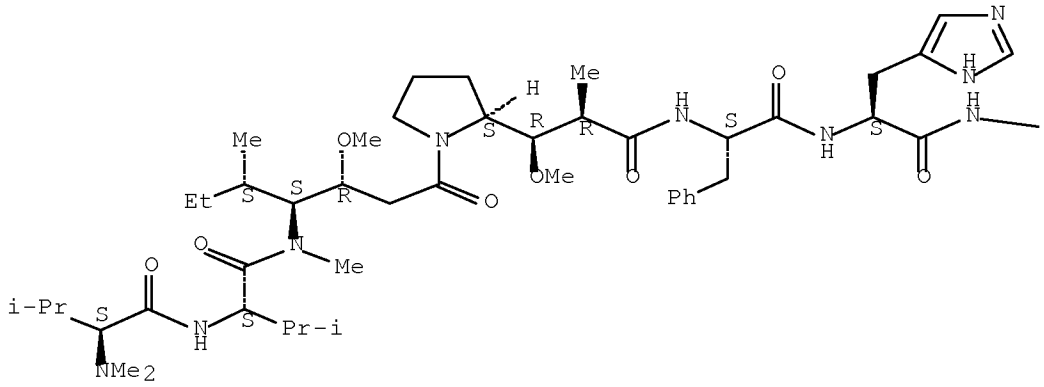
PAGE 1-B



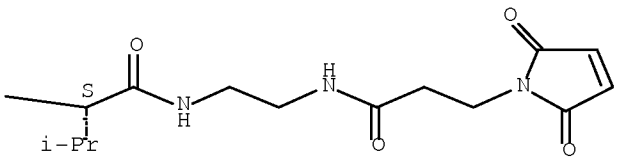
RN 1070273-55-0 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-histidyl-N-[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



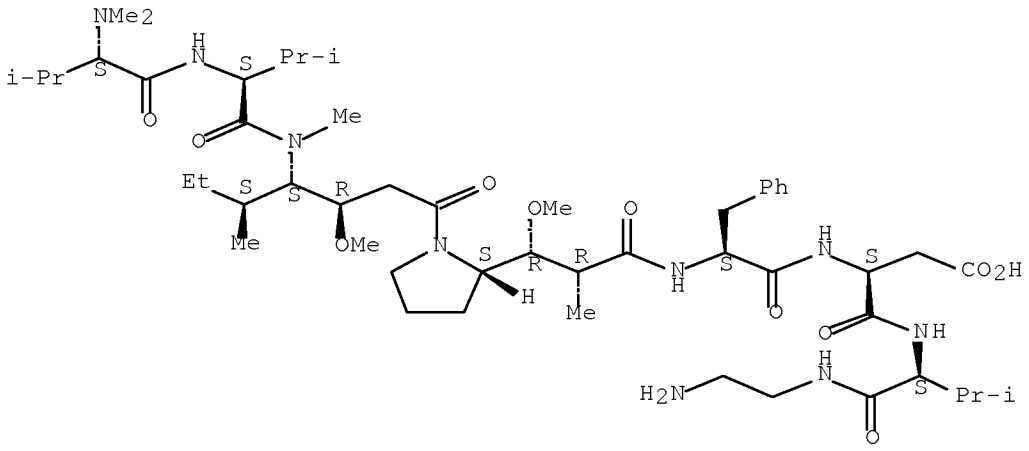
PAGE 1-B



IT 1070273-92-5P 1070273-94-7P 1070273-96-9P
1070273-98-1P 1070274-38-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(peptide linkers for highly potent antibody-auristatin conjugate)

RN 1070273-92-5 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-α-aspartyl-N-(2-aminoethyl)- (CA INDEX NAME)

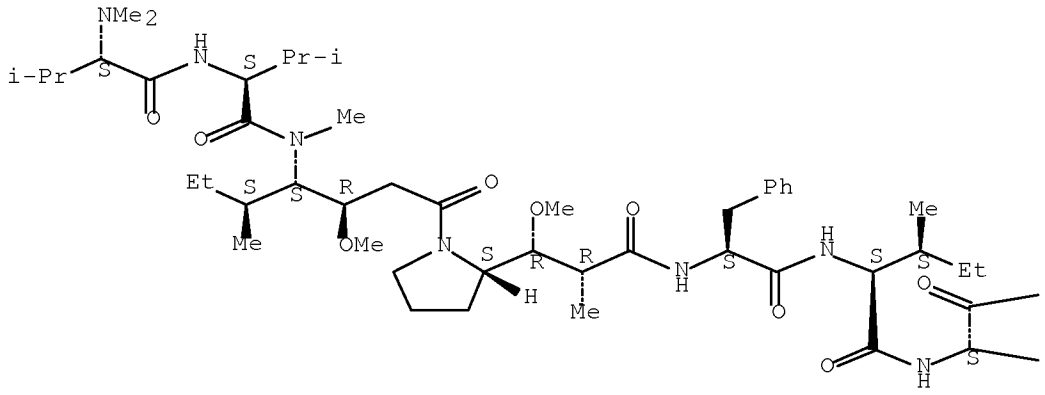
Absolute stereochemistry.



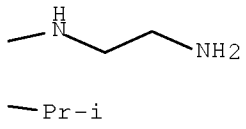
RN 1070273-94-7 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-isoleucyl-N-(2-aminoethyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



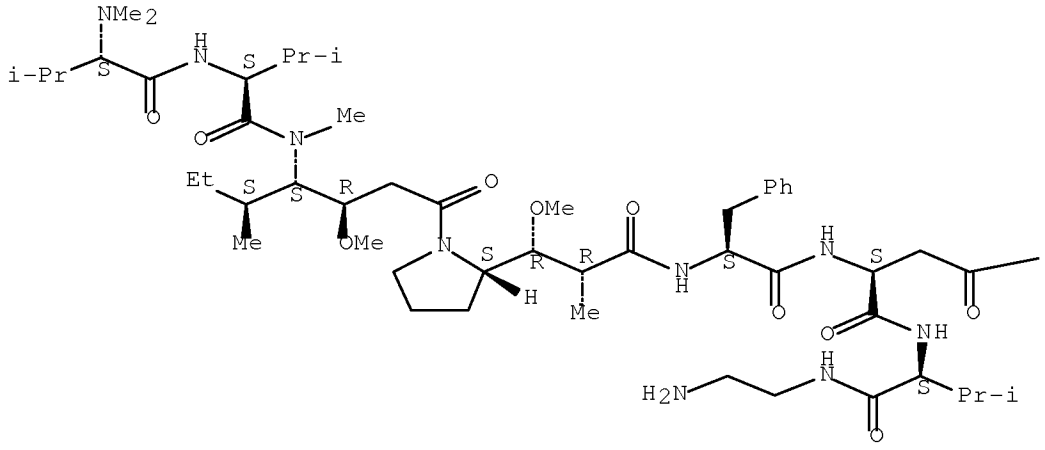
PAGE 1-B



RN 1070273-96-9 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-asparaginyl-N-(2-aminoethyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



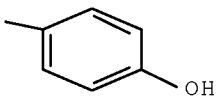
PAGE 1-B

RN 1070273-98-1 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-tyrosyl-N-(2-aminoethyl)- (CA INDEX NAME)

Absolute stereochemistry.

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

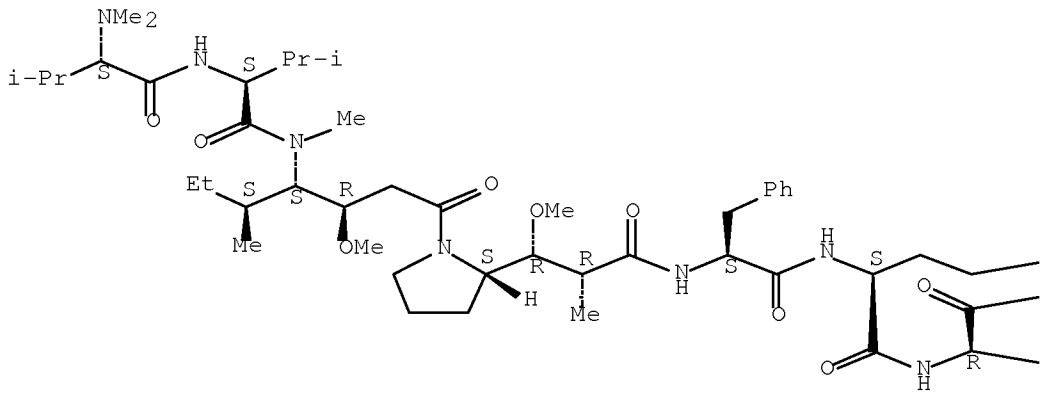
PAGE 1-B



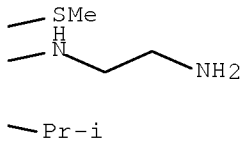
RN 1070274-38-2 HCAPLUS
CN D-Valinamide, N,N-dimethyl-L-valyl-L-valyl-(3R,4S,5S)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(αR,βR,2S)-β-methoxy-α-methyl-2-pyrrolidinepropanoyl-L-phenylalanyl-L-methionyl-N-(2-aminoethyl)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CC 1-6 (Pharmacology)
Section cross-reference(s): 34
ST antibody auristatin conjugate peptide linker antitumor agent neoplasm
IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TNFSF7 (tumor necrosis factor superfamily member 7); peptide linkers for highly potent antibody-auristatin conjugate)
IT Neuroglia, neoplasm
(glioblastoma; peptide linkers for highly potent antibody-auristatin conjugate)
IT Antitumor agents
Drug delivery systems
Human
Neoplasm
(peptide linkers for highly potent antibody-auristatin conjugate)
IT 876303-33-2DP, reaction products with cysteine thiol of IF6 antibody 1070273-51-6DP, reaction products with cysteine thiol of IF6 antibody 1070273-53-8DP, reaction products with cysteine thiol of IF6 antibody 1070273-55-0DP, reaction products with cysteine

thiol of IF6 antibody 1070273-57-2DP, reaction products with cysteine
thiol of IF6 antibody 1070273-59-4DP, reaction products with cysteine
thiol of IF6 antibody 1070273-61-8DP, reaction products with cysteine
thiol of IF6 antibody 1070273-63-0DP, reaction products with cysteine
thiol of IF6 antibody 1070273-65-2DP, reaction products with cysteine
thiol of IF6 antibody 1070273-67-4DP, reaction products with cysteine
thiol of IF6 antibody 1070273-69-6DP, reaction products with cysteine
thiol of IF6 antibody 1070273-71-0DP, reaction products with cysteine
thiol of IF6 antibody 1070273-74-3DP, reaction products with cysteine
thiol of IF6 antibody 1070273-76-5DP, reaction products with cysteine
thiol of IF6 antibody 1070273-78-7DP, reaction products with cysteine
thiol of IF6 antibody 1070273-80-1DP, reaction products with cysteine
thiol of IF6 antibody 1070273-82-3DP, reaction products with cysteine
thiol of IF6 antibody 1070273-84-5DP, reaction products with cysteine
thiol of IF6 antibody 1070273-86-7DP, reaction products with cysteine
thiol of IF6 antibody 1070273-88-9DP, reaction products with cysteine
thiol of IF6 antibody

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(peptide linkers for highly potent antibody-auristatin conjugate)

IT 1070273-92-5P 1070273-94-7P 1070273-96-9P
1070273-98-1P 1070274-00-8P 1070274-02-0P 1070274-04-2P
1070274-06-4P 1070274-08-6P 1070274-10-0P 1070274-12-2P
1070274-14-4P 1070274-16-6P 1070274-18-8P 1070274-20-2P
1070274-22-4P 1070274-24-6P 1070274-26-8P 1070274-28-0P
1070274-30-4P 1070274-32-6P 1070274-34-8P 1070274-36-0P
1070274-38-2P 1070274-40-6P 1070274-42-8P 1070274-44-0P
1070274-46-2P 1070274-48-4P 1070274-50-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(peptide linkers for highly potent antibody-auristatin conjugate)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 3 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1011219 HCAPLUS Full-text
DOCUMENT NUMBER: 149:288950
TITLE: Preparation of albumin-binding dual acting prodrugs containing a peptide cleavable linker useful in the diagnosis and treatment of diseases, especially neoplasm
INVENTOR(S): Kratz, Felix; Merfort, Irmgard
PATENT ASSIGNEE(S): KTB Tumorforschungsgesellschaft M.b.h., Germany
SOURCE: PCT Int. Appl., 35pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008098789	A2	20080821	WO 2008-EP1188	20080215

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2007-3342 A 20070216

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is related to a prodrug, e.g., I, which contains at least two different pharmaceutically and/or diagnostically active compds. independently bound by cleavable linkers and a protein-binding moiety which is capable of binding to carrier a mol. Thus, I was prepared by a multi-step synthesis using Cbz-Glu-OtBu, 6-maleimidocaproic acid chloride, paclitaxel and doxorubicin hydrochloride and bound in situ to albumin, thus enabling a more specific transport to the tumor tissue and releasing both doxorubicin and paclitaxel in tumor tissue and tumor cells. In a cytotoxicity assay against HT29 colon carcinoma cells prodrug I showed an IC50 value in the low nanomolar region (IC50 about 11 nM).

IT 1049627-53-3P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

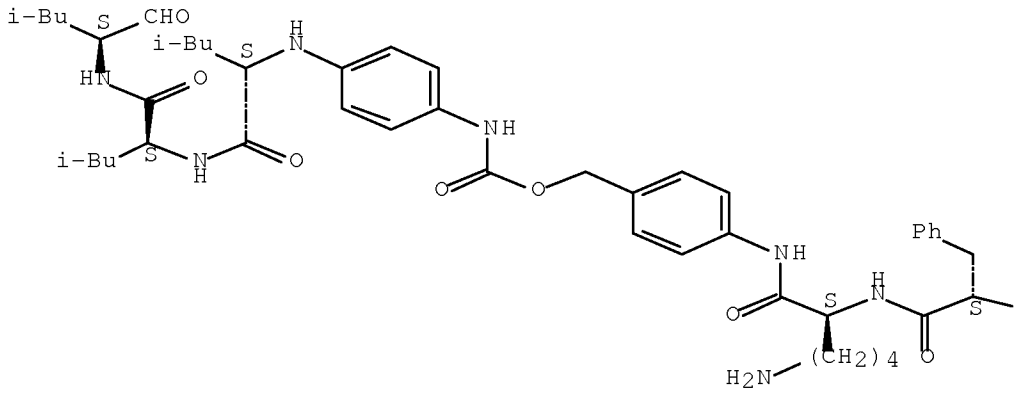
(preparation of albumin-binding dual acting prodrugs containing a peptide cleavable linker useful in diagnosis and treatment of neoplasm)

RN 1049627-53-3 HCAPLUS

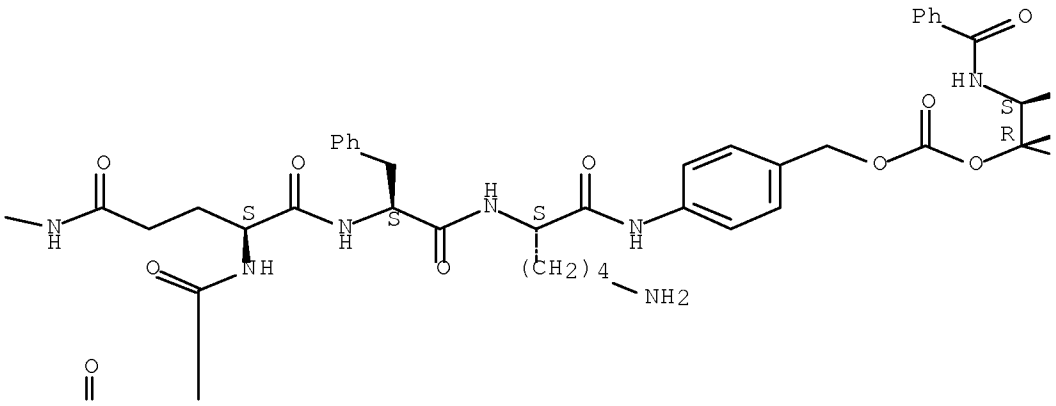
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-α-glutamyl-L-phenylalanyl-N-[4-[[[[(1R,2S)-2-(benzoylamino)-1-[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-2-phenylethoxy]carbonyl]oxy]methyl]phenyl]-, (1→1'')-amide with N-[4-[[[[4-[(L-phenylalanyl-L-lysyl)amino]phenyl]methoxy]carbonyl]amino]phenyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]-L-leucinamide (CA INDEX NAME)

Absolute stereochemistry.

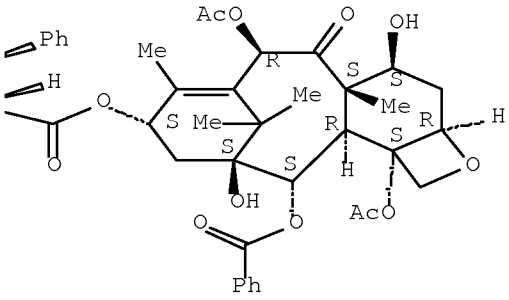
PAGE 1-A



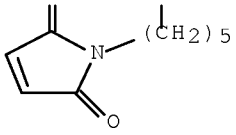
PAGE 1-B



PAGE 1-C



PAGE 2-B



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 26, 33, 63
IT Alkylating agents, biological
Analgesics
Angiogenesis inhibitors
Anti-infective agents
Anti-inflammatory agents
Antibiotics
Antipyretics
Antirheumatic agents
Antitumor agents
Antiviral agents
Autoimmune disease
Combination chemotherapy
Cytotoxic agents
Diagnosis
Disulfide group
Drug resistance modulators
Drug targets
Enzyme inhibitors
Fluorescent substances
Fungicides
Immunomodulators
Immunosuppressants
Infection
Light sources
Neoplasm
Pathogen
Pharmaceutical carriers
Prodrugs
Radioactive substances
Viral infection
(dual acting prodrugs useful in diagnosis and treatment of diseases)
IT Peptides, preparation
RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of albumin-binding dual acting prodrugs containing a peptide cleavable linker useful in diagnosis and treatment of neoplasm)
IT 82333-93-5P, 6-Maleimidocaproic chloride
RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of albumin-binding dual acting prodrugs containing a
peptide cleavable linker useful in diagnosis and treatment of neoplasm)
IT 118359-42-5P 118359-43-6P 1049627-38-4P 1049627-40-8P
1049627-43-1P 1049627-44-2P 1049627-46-4P 1049627-47-5P
1049627-48-6P 1049627-49-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of albumin-binding dual acting prodrugs containing a
peptide cleavable linker useful in diagnosis and treatment of neoplasm)
IT 1049627-51-1D, serum albumin-bound
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of albumin-binding dual acting prodrugs containing a peptide

cleavable linker useful in diagnosis and treatment of neoplasm
)

IT 1049627-50-0P 1049627-52-2P 1049627-53-3P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of albumin-binding dual acting prodrugs containing a peptide cleavable linker useful in diagnosis and treatment of neoplasm
)

IT 870-46-2, tert-Butyl carbazate 5070-13-3, Bis-p-nitrophenyl carbonate 5891-45-2 23429-44-9 25316-40-9, Doxorubicin hydrochloride 55750-53-3, 6-Maleimidocaproic acid 1049627-45-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of albumin-binding dual acting prodrugs containing a peptide cleavable linker useful in diagnosis and treatment of neoplasm
)

L76 ANSWER 4 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:395025 HCAPLUS Full-text
TITLE: Valepotriate-induced apoptosis of gastric cancer cell line MKN-45
AUTHOR(S): Ye, Jianming; Hu, Pinjin; Yi, Cuiqiong; Xue, Cunkuan; Hu, Chuangying; Chen, Fengming; Qian, Wei
CORPORATE SOURCE: Department of Gastroenterology, Zhongshan People's Hospital, Sun Yat-Sen University, Zhongshan, Guangdong Province, 528402, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2007), 15(1), 22-28
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Apoptosis of gastric cancer cell line MKN-45 induced by valepotriate and its relationship with the expressions of caspase, P53 and Survivin were studied. Gastric cancer cell line MKN-45 was divided into 4 groups, named group A (the control), B (treated with caspase-3, -8 and -9 inhibitors), C (treated with valepotriate) and D (treated with inhibitory agents plus valepotriate), resp. Apoptosis rates of MKN-45 cells were tested by fluorescence activated cell sorter (FACS) at different time (24, 48 and 72 h) in each group. After exposure to different concns. of valepotriate for different time (12, 24, 48 and 72 h), MKN-45 cells were collected, and RNA was extracted by tripure agent. The mRNA expression of Survivin was assayed by reverse transcription-polymerase chain reaction (RT-PCR), while the protein expression of P53 and Survivin were detected by immunohistochem. methods 24 h after exposure to different concns. of valepotriate (50 and 100 mg/L). Apoptosis rates of MKN-45 cells were not significantly different between group A and B at 24, 48 and 72 h ($P>0.05$). Apoptosis rates were significantly higher in MKN-45 cells exposed to valepotriate plus caspase-3 inhibitor or caspase-9 inhibitor for 24, 48 and 72 h than those in group A (24 h: 5.73%, 5.41% vs. 4.38%, $P<0.01$; 48 h: 6.88%, 6.32% vs. 4.35%, $P<0.01$; 72 h: 7.72%, 8.62% vs. 4.54%, $P<0.01$), but lower than those in group C (24 h: 5.73%, 5.41% vs. 8.14%, $P<0.01$; 48 h: 6.88%, 6.32% vs. 12.31%, $P<0.01$; 72 h: 7.72%, 8.62% vs. 26.41%, $P<0.01$). Apoptosis rates of MKN-45 cells exposed to valepotriate plus caspase-8 inhibitor for 24, 48 and 72 h were notably increased in comparison with those in group A (8.02% vs. 4.38%, $P<0.01$; 11.05% vs. 4.35%, $P<0.01$; 24.86% vs. 4.54%, $P<0.01$), but was not significantly different from those in group C ($P>0.05$). Valepotriate down-regulated the expression of Survivin mRNA in MKN-45 cells in both concentration- and time-dependent manner. Valepotriate also down-regulated the expression of Survivin protein but up-regulated the expression of P53 protein in MKN-45 cells in a concentration-dependent way. Valepotriate-induced apoptosis of MKN-45 cells was correlated with the high

expression of P53 protein and low expression of Survivin mRNA and protein, and it could be inhibited by caspase-3 inhibitor or caspase-9 inhibitor, but not by caspase-8 inhibitor.

IT INDEXING IN PROGRESS

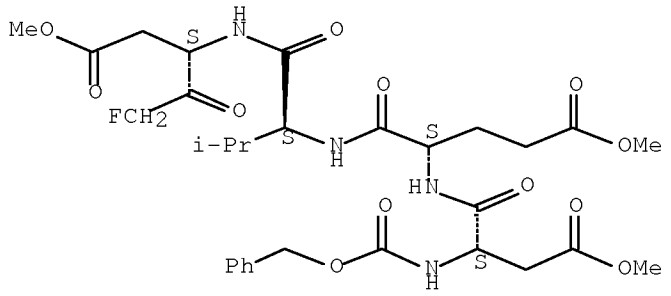
IT 210344-95-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1 (Pharmacology)

ST valepotriate caspase inhibitor survivin p53 apoptosis stomach neoplasm

IT Stomach, neoplasm
(carcinoma; valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

IT Carcinoma, neoplasm
(gastric; valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

IT Antitumor agents
Apoptosis
Natural products, pharmaceutical
Valeriana glechomifolia
(valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

IT p53 (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

IT 169592-56-7, Apopain 179241-78-2 180189-96-2 210344-95-9 210344-98-2 210345-04-3 371761-91-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(valepotriate-induced apoptosis of gastric cancer cell line MKN-45 and relationship of valepotriate with caspase, p53 and survivin)

L76 ANSWER 5 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:70903 HCAPLUS Full-text
DOCUMENT NUMBER: 148:138338

TITLE: Peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging
INVENTOR(S): Bogyo, Matthew; Berger, Alicia B.
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 105pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008008264	A2	20080117	WO 2007-US15516	20070706
WO 2008008264	A3	20081120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2007273035	A1	20080117	AU 2007-273035	20070706
PRIORITY APPLN. INFO.:			US 2006-819233P P	20060707
			WO 2007-US15516 W	20070706

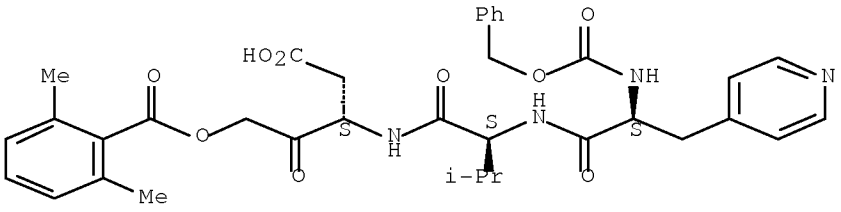
OTHER SOURCE(S): MARPAT 148:138338

AB Described here are novel, highly selective inhibitors and activity based probes (ABPs) for caspases 3, 7, 8, and 9 and legumain. The compds. selectively inhibit only certain caspases. A positional scanning combinatorial library (PSCL) approach was used to screen pools of peptide acyloxymethyl ketones (AOMKs) containing both natural and non-natural amino acids for activity against a number of purified recombinant caspases. These screens were used to identify structural elements at multiple positions on the peptide scaffold that could be modulated to control inhibitor specificity towards target caspases. Further disclosed are AOMK conjugates with labels, e.g., fluorophores, metal-chelating groups, etc., which may be used in imaging.

IT 1006596-48-0 1006596-51-5
RL: ARG (Analytical reagent use); PRPH (Prophetic); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging)

RN 1006596-48-0 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-3-(4-pyridinyl)-L-alanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

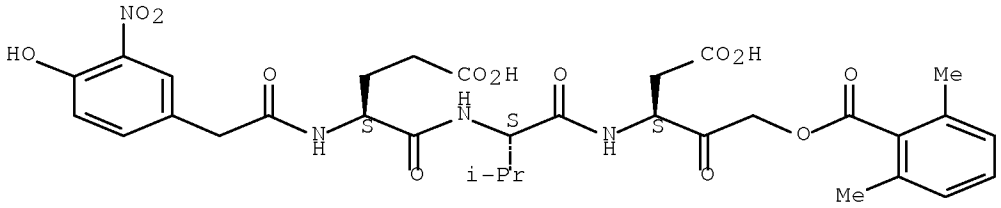
Absolute stereochemistry.



RN 1006596-51-5 HCAPLUS

CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-glutamyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.



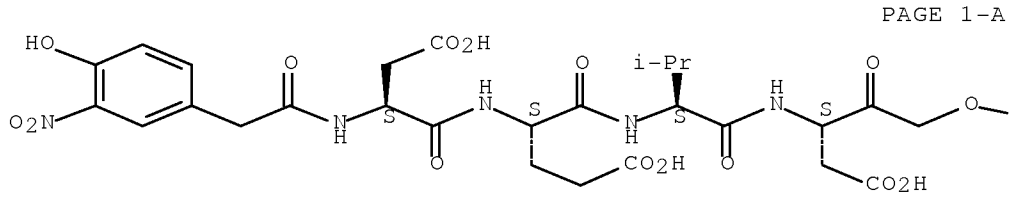
IT 913253-09-5 913253-11-9 913253-12-0
913253-13-1 913253-14-2 1001059-48-8
1001059-50-2 1001059-60-4 1001059-61-5
1001060-19-0
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging)

RN 913253-09-5 HCAPLUS

CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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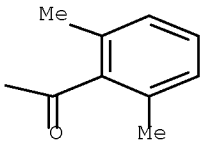
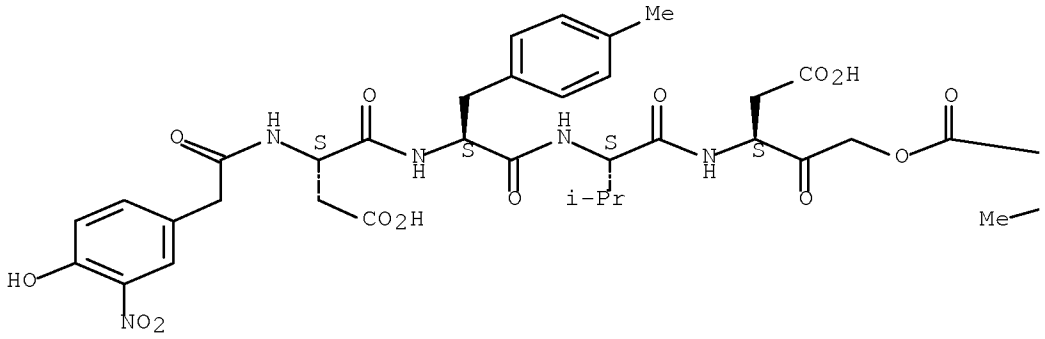


RN 913253-11-9 HCAPLUS

CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-aspartyl-4-methyl-L-phenylalanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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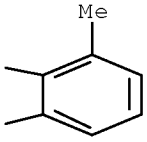
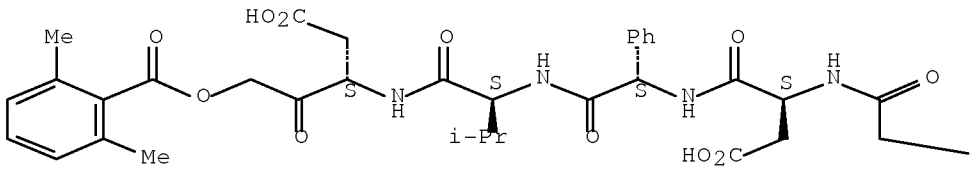


RN 913253-12-0 HCAPLUS

CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-aspartyl-(2S)-2-phenylglycyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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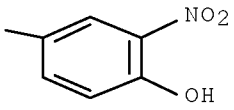
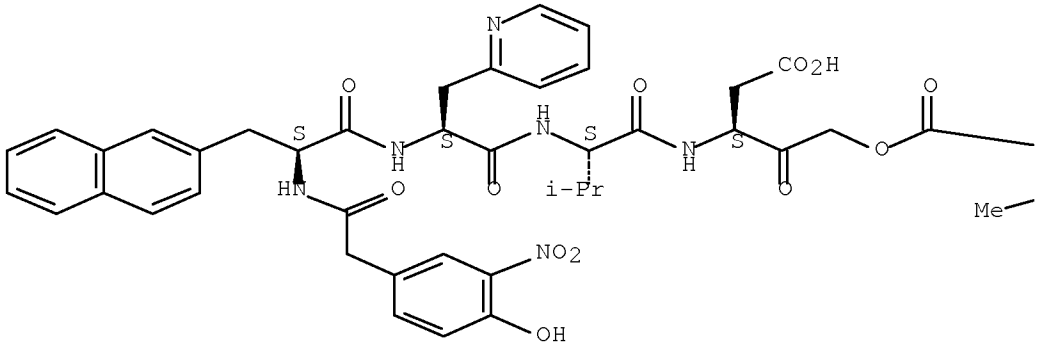


RN 913253-13-1 HCAPLUS
CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-3-(2-naphthalenyl)-L-alanyl-3-(2-pyridinyl)-L-alanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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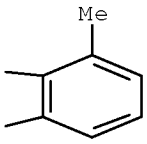
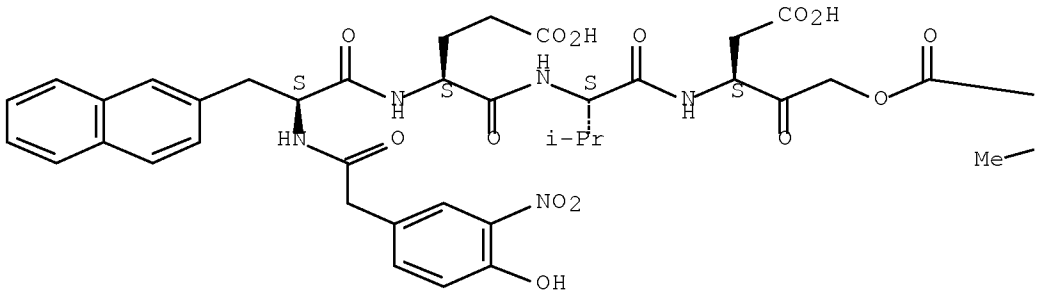


RN 913253-14-2 HCAPLUS
CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-3-(2-naphthalenyl)-L-alanyl-L-α-glutamyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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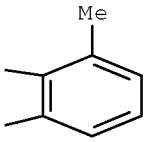
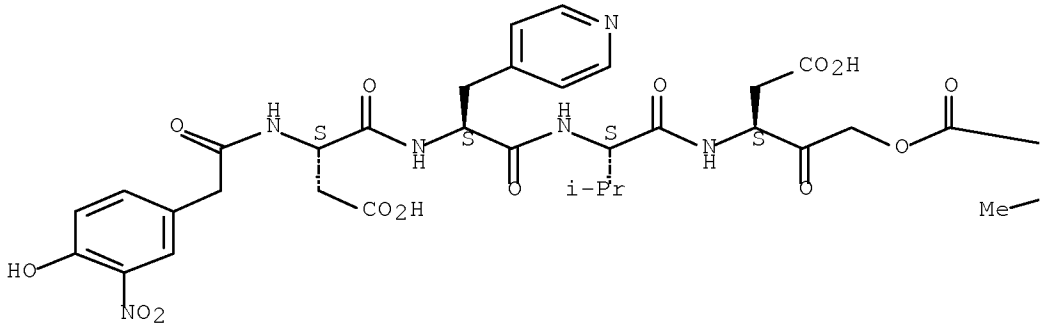


RN 1001059-48-8 HCAPLUS
CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-aspartyl-3-(4-pyridinyl)-L-alanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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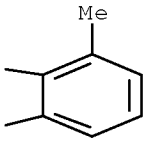
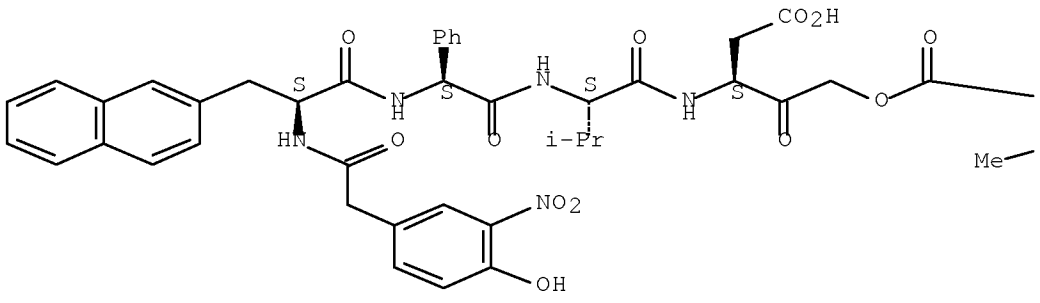


RN 1001059-50-2 HCAPLUS
CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-3-(2-naphthalenyl)-L-alanyl-(2S)-2-phenylglycyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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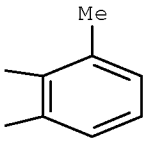
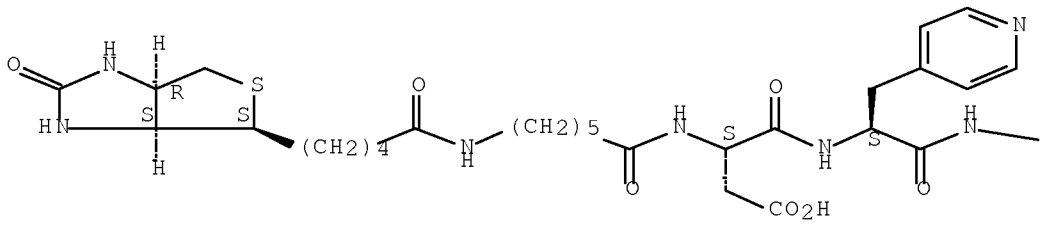


RN 1001059-60-4 HCAPLUS
CN L-Valinamide, N-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-L-α-asparty1-3-(4-pyridinyl)-L-alanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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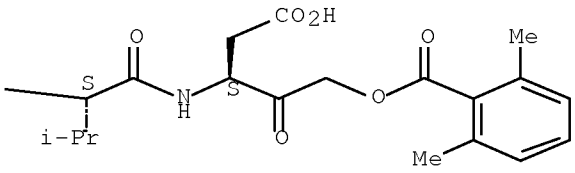
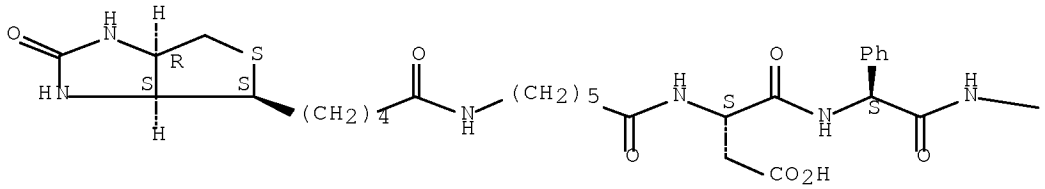


RN 1001059-61-5 HCAPLUS
CN L-Valinamide, N-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-L-α-asparty1-(2S)-2-phenylglycyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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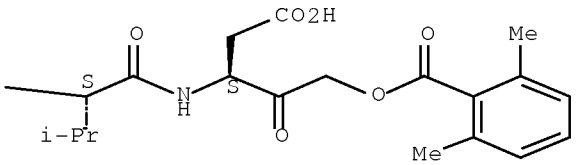
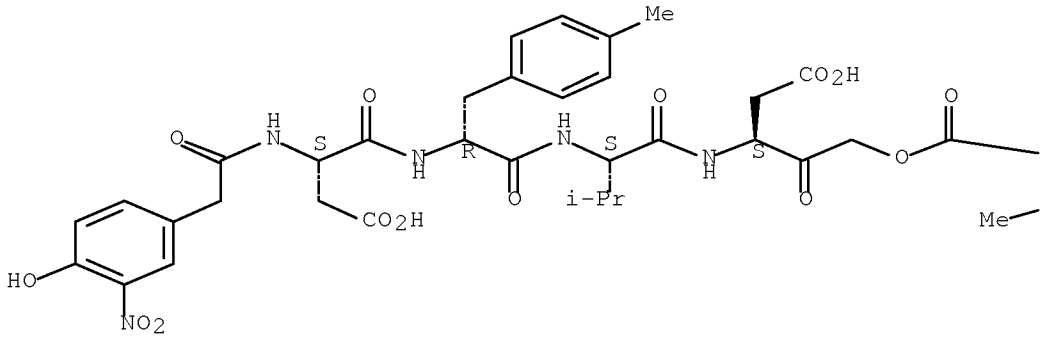


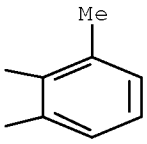
RN 1001060-19-0 HCAPLUS

CN L-Valinamide, N-[2-(4-hydroxy-3-nitrophenyl)acetyl]-L-α-aspartyl-4-methyl-D-phenylalanyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





CC 7-3 (Enzymes)
Section cross-reference(s): 1, 9
IT Animalia
Animals
Antitumor agents
Human
Imaging
Neoplasm
(peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging)
IT 1006596-31-1 1006596-32-2 1006596-33-3 1006596-34-4 1006596-35-5
1006596-36-6 1006596-37-7 1006596-38-8 1006596-39-9 1006596-40-2
1006596-41-3 1006596-42-4 1006596-43-5 1006596-44-6 1006596-45-7
1006596-46-8 1006596-47-9 1006596-48-0 1006596-49-1
1006596-50-4 1006596-51-5 1006596-52-6 1006596-53-7
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1006596-59-3 1006596-60-6 1006596-61-7 1006596-62-8 1006596-63-9
1006596-64-0 1006596-65-1 1006596-66-2 1006596-67-3 1006596-68-4
1006596-69-5 1006596-70-8 1006596-71-9
RL: ARG (Analytical reagent use); PRPH (Prophetic); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging)
IT 913253-07-3 913253-09-5 913253-11-9
913253-12-0 913253-13-1 913253-14-2
913253-15-3 913253-16-4 913253-20-0 913253-21-1 913253-22-2
913253-23-3 1001059-48-8 1001059-49-9 1001059-50-2
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1001059-60-4 1001059-61-5 1001059-62-6 1001059-63-7
1001059-64-8 1001059-65-9 1001059-66-0 1001060-19-0
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(peptide acyloxymethyl ketones selectively inhibiting caspases and their use in therapy and imaging)

L76 ANSWER 6 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:548499 HCAPLUS Full-text
DOCUMENT NUMBER: 147:109330
TITLE: Expression level of Bcl-XL critically affects sensitivity of hepatocellular carcinoma cells to LIGHT-enhanced and interferon-γ-induced apoptosis
AUTHOR(S): Li, Jun; Shen, Feng; Wu, Dong; Wei, Li-Xin; Wang, Yi-Zhen; Shi, Le-Hua; Zou, Ying; Wu, Meng-Chao
CORPORATE SOURCE: Division of Comprehensive Treatment, Eastern Hepatobiliary Hospital, Eastern Hepatobiliary

Institute, Second Military Medical University, Shanghai, 200438, Peop. Rep. China
SOURCE: Oncology Reports (2007), 17(5), 1067-1075
CODEN: OCRPEW; ISSN: 1021-335X
PUBLISHER: Oncology Reports
DOCUMENT TYPE: Journal
LANGUAGE: English

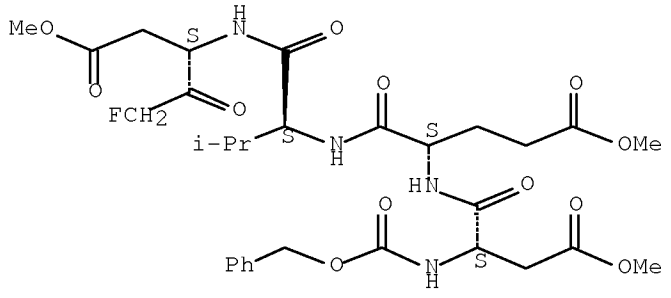
AB The mol. mechanisms of apoptosis caused by IFN-γ (interferon gamma)/LIGHT (lymphotoxin-related inducible ligand that competes for glycoprotein D binding to herpes virus entry mediator on T cells) have not been studied in detail. The present study was undertaken to gain insights into the signaling pathways involved in apoptosis induced by IFN-γ/LIGHT in hepatocellular carcinoma (HCC) cell lines. Cell proliferation assay, flow cytometry, Western blotting, gene transfer and RNA interference were used in this study. LIGHT enhanced IFN-γ-mediated apoptosis in Hep3B cells. IFN-γ/LIGHT-induced apoptosis was inhibited by blocking peptides to the lymphotoxin β receptor (LT-β R), and not by the herpes virus entry mediator (HVEM). Expression of LT-β R remained unchanged after cytokine treatments. IFN-γ/LIGHT treatment resulted in the down-regulation of Bcl-XL and the activation of caspase-9 and caspase-3 as well as the decrease of phosphorylation of STAT3. HepG2 and SMMC-7721 cells, which showed high levels of endogenous Bcl-XL, displayed resistance to IFN-γ/LIGHT-induced apoptosis. Overexpression of Bcl-XL in Hep3B cells increased the resistance to IFN-γ/LIGHT induced apoptosis while the down-regulation of Bcl-XL in HepG2 and SMMC-7721 cells by RNA interference decreased the resistance. Our study provides important mechanistic insights into IFN-γ/LIGHT-induced apoptosis in HCC cells and may help to select better therapeutic strategies for certain cancers with distinct Bcl-XL expression.

IT 210344-95-9
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
Section cross-reference(s): 15

ST BclXL LIGHT interferon IFNgamma anticancer apoptosis hepatocellular

carcinoma signaling
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bak; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-xL; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bid; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HveA (herpes virus entry mediator A); effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Ligands
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LIGHT; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Transcription factor STAT
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(STAT3; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Drug resistance
(antitumor; Aeffect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Antitumor agents
Apoptosis
Human
Phosphorylation, biological
RNA interference
Signal transduction
(effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Carcinoma
(hepatocellular; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Liver, neoplasm
(hepatoma; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Antitumor agents
(resistance to; Aeffect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)
IT Lymphokine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-lymphotoxin; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)

IT Interferons
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ; effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)

IT 169592-56-7, Caspase-3 179241-78-2, Caspase-8 180189-96-2, Caspase-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)

IT 210344-95-9 210344-98-2 210345-04-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effect of Bcl-XL expression on sensitivity of hepatocellular carcinoma to LIGHT-enhanced and interferon-γ-induced apoptosis)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 7 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:463352 HCAPLUS Full-text
DOCUMENT NUMBER: 146:462511
TITLE: Fibrin targeted therapeutics, particularly peptidomimetics, their preparation and use in the treatment of thromboembolism, infection, and cancer
INVENTOR(S): McMurry, Thomas J.; Kolodziej, Andrew; Carpenter, Alan P., Jr.; Jones, Simon; Graham, Philip; Looby, Richard; Shrikumar, A. Nair; Wang, Xifang; Overoye-Chen, Kirsten; Barrett, John A.
PATENT ASSIGNEE(S): Epix Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 136pp.
CODEN: PIXXD2
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PATENT INFORMATION:

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WO 2007047608	A2	20070426	WO 2006-US40430	20061016
WO 2007047608	A3	20070920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20070111947 A1 20070517 US 2006-581677 20061016
PRIORITY APPLN. INFO.: US 2005-726632P P 20051014
US 2006-800152P P 20060512
OTHER SOURCE(S): MARPAT 146:462511
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

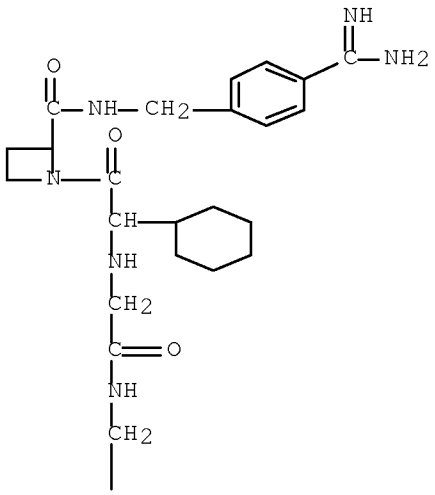
AB The invention is related to hybrid mols. of formula [D]m-[L]n-[F]q [I; wherein [D] comprises a bioactive moiety for treating thromboembolism, infection, and cancer; [L] comprises a linker moiety; [F] comprises a fibrin-targeting moiety selected from a peptide, peptidomimetic, or a small mol.; m, q = independently 1-20; n = 0-20]. I can provide enhanced efficacy and reduced systemic toxicity relative to a corresponding non-targeted bioactive mol. Thus, a paclitaxel-fibrin binding peptide conjugate II was prepared using paclitaxel, succinyl anhydride, and peptide III (H-R). II in a dose-responsive manner caused a significant decrease in the number of cancer cells in lung and breast cancer lines and in the number of smooth muscle and endothelial cells.

IT 935546-52-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

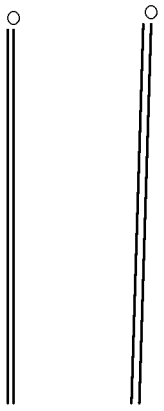
RN 935546-52-4 HCAPLUS

CN Yttrate(6-), [μ-[N-[(1R)-2-[(2S)-2-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-1-azetidinyl]-1-cyclohexyl-2-oxoethyl]glycyl-2-[2-(2-aminoethoxy)ethoxy]acetyl-L-α-aspartyl-L-tyrosyl-D-α-glutamyl-L-cysteinyl-(4R)-4-hydroxy-L-prolyl-3-iodo-L-tyrosylglycyl-L-leucyl-L-cysteinyl-L-histidyl-L-isoleucyl-N-[[4-[(4S,11S)-4-[[(4S)-4-[bis[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]amino-κN]-4-(carboxy-κO)-1-oxobutyl]amino]-12-[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]-11,16-di(carboxy-κO)-15-[(carboxy-κO)methyl]-3,8-dioxo-2,7,12,15-tetraazahexadec-1-yl-κN12,κN15]phenyl]methyl]-L-leucinamide cyclic (6→11)-disulfidato(12-)]]di-, hydrogen (1:2) (CA INDEX NAME)

PAGE 1-C



PAGE 2-B



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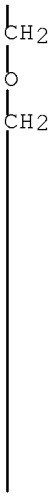

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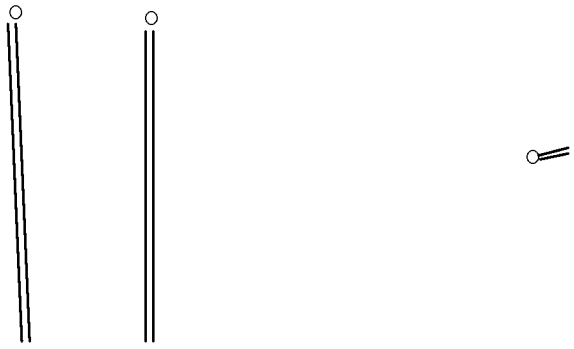

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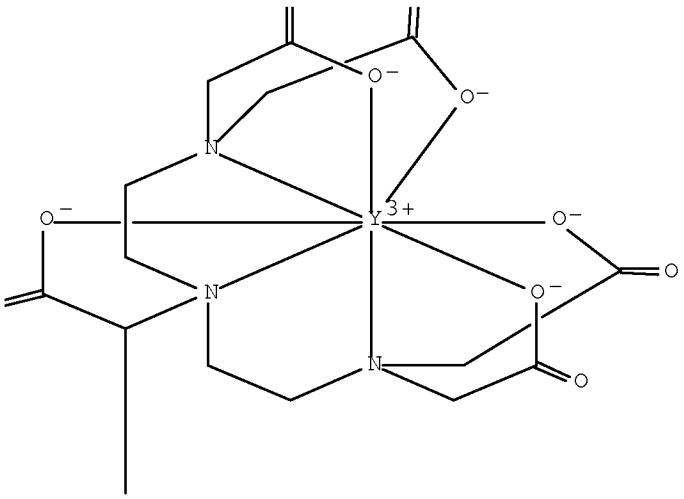

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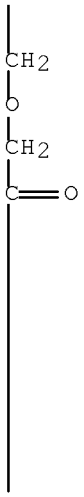

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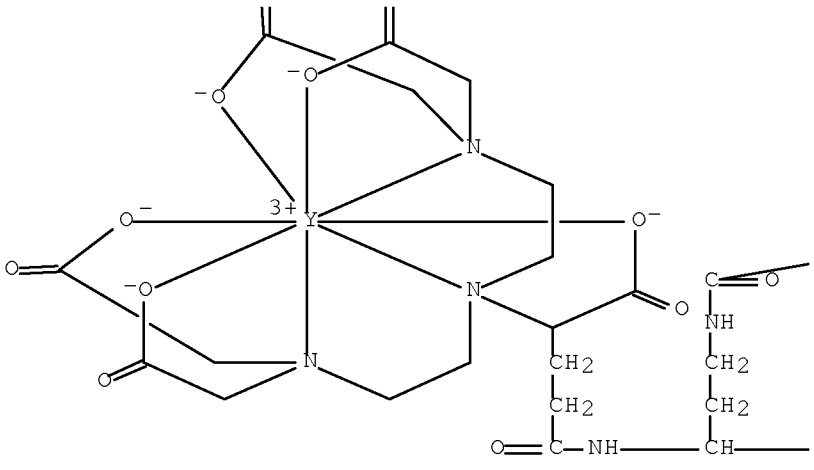

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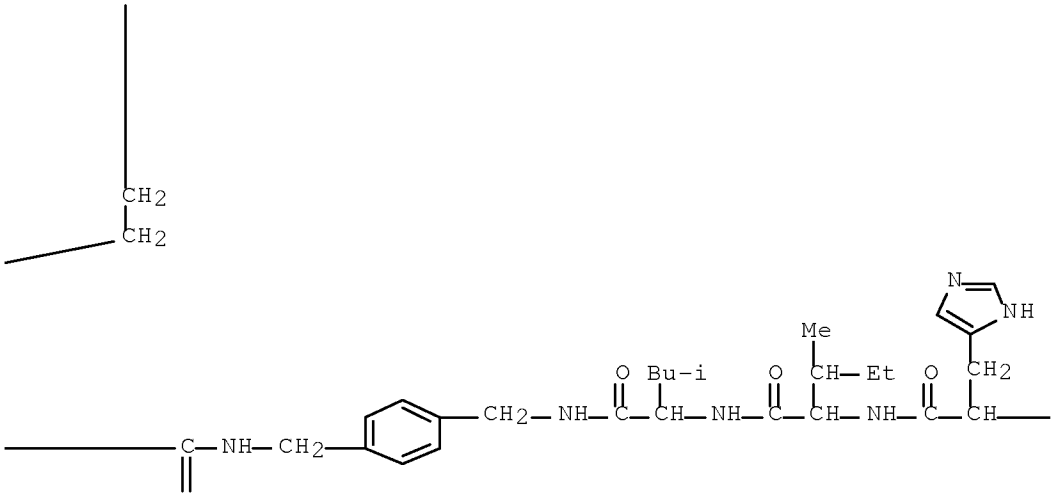

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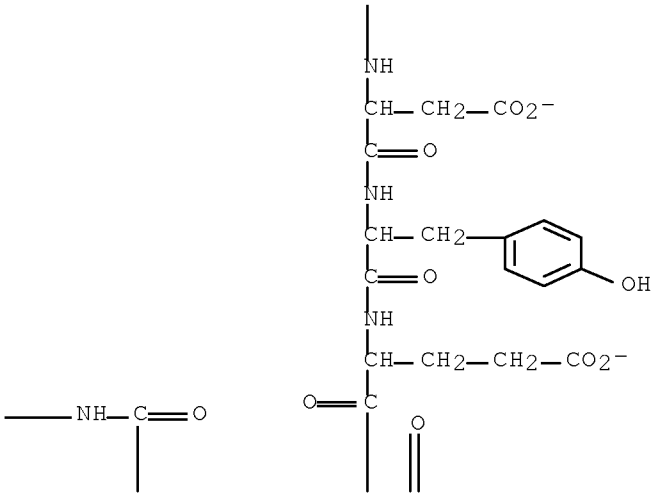
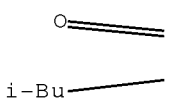


PAGE 5-A

PAGE 5-B



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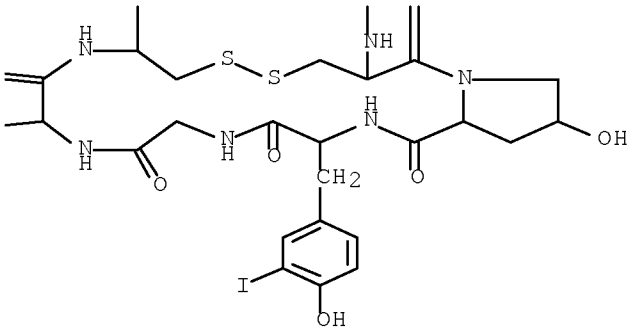

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 30, 33, 63
ST peptidomimetic fibrin targeted therapeutic prepn thromboembolism infection cancer
IT Growth factor receptors
Tyrosine kinase receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Axl, Sky inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)
IT Growth factor receptors
Tyrosine kinase receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Axl, inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)
IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD40-L (antigen CD40 ligand), inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents
useful in treatment of thromboembolism, infection, and cancer)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GAS6 (growth arrest-specific 6), inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents
useful in treatment of thromboembolism, infection, and cancer)
IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P-, inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)
IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PSGL-1 (P-selectin glycoprotein ligand-1), inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)
IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(P2T, inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Cytotoxic agents
(antimetabolites, bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Thrombosis
(arterial; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Alkylating agents, biological
Antibiotics
Cytotoxic agents
Natural products
Platelet aggregation inhibitors
Radiopharmaceuticals
(bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Fibrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Coordination compounds
Glycopeptides
Macrolides
Quinolones
Radionuclides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Toxins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxins; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Pharmaceutical injections
(i.p. injections; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Pharmaceutical injections
(i.v. injections; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT RANTES (chemokine)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT CD40 (antigen)
Fibrinogen receptors
Thrombin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; bioconjugates with fibrin-targeting moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Anesthetics
(local; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Anti-infective agents

Anticoagulants
Antitumor agents
Buffers
Coloring materials
Fibrinolytics
Flavoring materials
Human
Infection
Infectious endocarditis
Neoplasm
Oral drug delivery systems
Oryctolagus cuniculus
Peptidomimetics
Pharmaceutical excipients
Pharmaceutical liposomes
Preservatives
Rabbit
Salivary gland
Solubilizers
Thrombolytics
Thromboxane receptor antagonists
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Blood-coagulation factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Peptides, preparation
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Aminoglycosides
Prostate-specific antigen
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Pharmaceutical injections
(s.c. injections; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Embolism
(thromboembolism; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tick anticoagulation; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Chiroptera
(vampire bat; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Thrombosis
(venous; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, inhibitors; bioconjugates with fibrin-targeting

moieties; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT Antibiotics
(β-lactam; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 9002-01-1D, Streptokinase, plasminogen activator complexes; bioconjugates with fibrin-targeting moieties
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anisolated; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 116036-70-5D, Fibrolase, bioconjugate with fibrin-targeting moieties
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(copperhead snake; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 139466-48-1D, bioconjugate with fibrin-targeting moieties 142243-03-6D, bioconjugate with fibrin-targeting moieties
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 9001-92-7, Proteinase 9002-04-4D, Thrombin, inhibitors; bioconjugates with fibrin-targeting moieties 9002-05-5D, Factor Xa, inhibitors; bioconjugates with fibrin-targeting moieties 9004-06-2, Neutrophil elastase 9025-82-5D, Phosphodiesterase, inhibitors; bioconjugates with fibrin-targeting moieties 9031-56-5D, Synthetase, inhibitors; bioconjugates with fibrin-targeting moieties 35121-78-9D, Prostacyclin, mimetics; bioconjugate with fibrin-targeting moietiess 37203-61-5D, Factor XIa, inhibitors; bioconjugates with fibrin-targeting moieties 37203-62-6D, Factor XIIa, inhibitors; bioconjugates with fibrin-targeting moieties 37316-87-3D, Factor IXa, inhibitors; bioconjugates with fibrin-targeting moieties 65312-43-8D, Factor VIIa, inhibitors; bioconjugates with fibrin-targeting moieties 65522-14-7D, Blood-coagulation factor Va, inhibitors; bioconjugates with fibrin-targeting moieties 138757-15-0D, α2-Antiplasmin, inhibitors; bioconjugates with fibrin-targeting moieties 140208-23-7D, bioconjugate with fibrin-targeting moieties 141907-41-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 935546-52-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 519-23-3DP, bioconjugate with fibrin-targeting moieties 20830-81-3DP, bioconjugate with fibrin-targeting moieties 23214-92-8DP, bioconjugate with fibrin-targeting moieties 33069-62-4DP, bioconjugate with fibrin-targeting moieties 51131-85-2DP, bioconjugate with fibrin-targeting moieties 101204-49-3DP, bioconjugate with fibrin-targeting moieties 143120-27-8DP, bioconjugate with fibrin-targeting moieties 144494-65-5DP, bioconjugate with fibrin-targeting moieties 150612-55-8DP, bioconjugate with fibrin-targeting moieties 155204-81-2DP, bioconjugate with fibrin-targeting moieties 183304-55-4DP, bioconjugate with fibrin-targeting moieties 186304-04-1DP, bioconjugate with fibrin-targeting moieties 192939-46-1DP, bioconjugate with fibrin-targeting moieties 209954-52-9DP, bioconjugate with fibrin-targeting moieties 211915-06-9DP, bioconjugate with

fibrin-targeting moieties 219672-29-4DP, bioconjugate with
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fibrin-targeting moieties 935546-51-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of
thromboembolism, infection, and cancer)

IT 50-59-9D, Cephaloridine, bioconjugate with fibrin-targeting moieties
50-78-2D, Aspirin, bioconjugate with fibrin-targeting moieties 56-75-7D,
Chloramphenicol, bioconjugate with fibrin-targeting moieties 57-66-9D,
Probenecid, bioconjugate with fibrin-targeting moieties 57-92-1D,
Streptomycin, bioconjugate with fibrin-targeting moieties 59-01-8D,
Kanamycin, bioconjugate with fibrin-targeting moieties 60-54-8D,
Tetracycline, bioconjugate with fibrin-targeting moieties 61-32-5D,
Methicillin, bioconjugate with fibrin-targeting moieties 61-33-6D,
bioconjugate with fibrin-targeting moieties 63-74-1D, Sulfonamide,
bioconjugate with fibrin-targeting moieties 66-79-5D, Oxacillin,
bioconjugate with fibrin-targeting moieties 69-53-4D, Ampicillin,
bioconjugate with fibrin-targeting moieties 81-81-2D, Warfarin,
bioconjugate with fibrin-targeting moieties 114-07-8D, Erythromycin,
bioconjugate with fibrin-targeting moieties 147-52-4D, Nafcillin,
bioconjugate with fibrin-targeting moieties 153-61-7D, Cephalothin,
bioconjugate with fibrin-targeting moieties 738-70-5D, Trimethoprim,
bioconjugate with fibrin-targeting moieties 1404-90-6D, Vancomycin,
bioconjugate with fibrin-targeting moieties 5935-65-9D,
Deacetylcephalothin, bioconjugate with fibrin-targeting moieties
7440-06-4D, Platinum, coordination complexes; bioconjugates with
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 108-30-5, Succinic anhydride, reactions 771-61-9, Pentafluorophenol 33069-62-4, Paclitaxel 935535-59-4D, resin-bound 935535-63-0, Melagatran 935535-66-3D, resin-bound 935535-67-4D, resin-bound 935535-72-1D, resin-bound 935535-74-3 935535-76-5 935535-77-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 935535-60-7P 935535-61-8P 935535-64-1P 935535-65-2P 935535-68-5P 935535-69-6P 935535-70-9P 935535-73-2P 935535-75-4P 935547-75-4P 935547-76-5P 935547-77-6P 935547-78-7P 935547-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 238099-75-7D, Thrombin activatable fibrinolysis inhibitor, bioconjugate with fibrin-targeting moieties
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

IT 115926-52-8D, Phosphoinositide-3-kinase, inhibitors; bioconjugates with

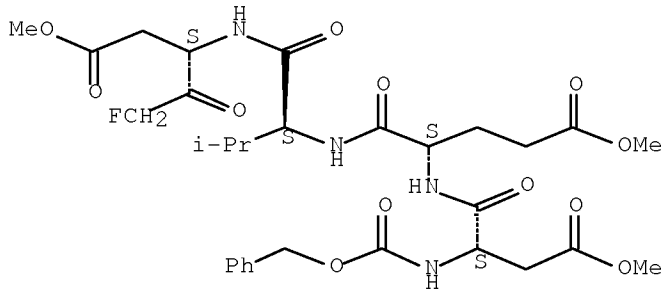
fibrin-targeting moieties
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β and γ isoforms; preparation of fibrin targeted therapeutic agents useful in treatment of thromboembolism, infection, and cancer)

L76 ANSWER 8 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:211194 HCAPLUS Full-text
DOCUMENT NUMBER: 146:350781
TITLE: Induction of apoptosis by d-limonene is mediated by a caspase-dependent mitochondrial death pathway in human leukemia cells
AUTHOR(S): Ji, Jun; Zhang, Li; Wu, Yuan-Yuan; Zhu, Xiao-Yu; Lv, Su-Qing; Sun, Xi-Zuo
CORPORATE SOURCE: Department of Central Laboratory, Dalian Municipal Central Hospital, Dalian, Peop. Rep. China
SOURCE: Leukemia & Lymphoma (2006), 47(12), 2617-2624
CODEN: LELYEA; ISSN: 1042-8194
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using K562 and HL60 cell lines, we have investigated the anti- tumoral activity of d-limonene, a monocyclic monoterpene, in human leukemia cells. Apoptosis was evaluated by Hoechst staining and by the annexin V/propidium iodide binding assay. D-Limonene induced apoptosis in a dose- and time-dependent manner in both cell lines. Our findings and data, demonstrating an increase in Bax protein expression, the release of cytochrome c from mitochondria, and an increase in caspase-9 and cleaved caspase-3, but not caspase-8, after the treatment of d-limonene, all suggest that the mitochondrial death pathway is primarily involved in the development of d-limonene-induced apoptosis.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(broad-spectrum caspase inhibitors z-VAD-fmk and z-DEVD-fmk inhibited d-limonene-induced apoptosis in human leukemia cell indicating that d-limonene induced apoptosis in caspase-dependent mitochondrial death pathway)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.

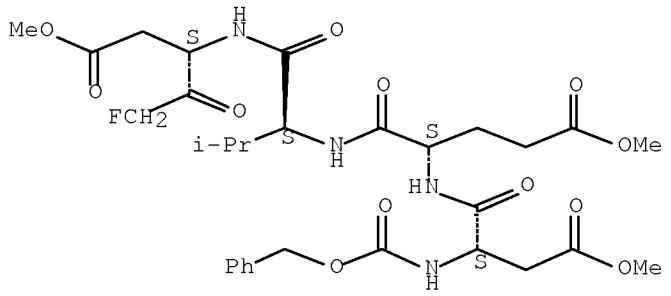


CC 1-6 (Pharmacology)

IT 187389-52-2 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(broad-spectrum caspase inhibitors z-VAD-fmk and z-DEVD-fmk inhibited d-limonene-induced apoptosis in human leukemia cell indicating that d-limonene induced apoptosis in caspase-dependent mitochondrial death pathway)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 9 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:198905 HCAPLUS Full-text
DOCUMENT NUMBER: 147:136584
TITLE: Fluorescence resonance energy transfer analysis of bid activation in living cells during ultraviolet-induced apoptosis
AUTHOR(S): Wu, Yinyuan; Xing, Da; Liu, Lei; Chen, Tongsheng; Chen, Wei R.
CORPORATE SOURCE: MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, South China Normal University, Guangzhou, 510631, Peop. Rep. China
SOURCE: Acta Biochimica et Biophysica Sinica (2007), 39(1), 37-45
CODEN: ABBSC2; ISSN: 1672-9145
PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB UV irradiation is a DNA-damaging agent that triggers apoptosis through both the membrane death receptor and mitochondrial apoptotic signaling pathways. Bid, a pro-apoptotic Bcl-2 family member, is important in most cell types to apoptosis in response to DNA damage. In this study, a recombinant plasmid, YFP-Bid-CFP, comprised of yellow and cyan fluorescent protein and a full length Bid, was used as a fluorescence resonance energy transfer anal. (FRET) probe. Using the FRET technique based on YFP-Bid-CFP, we found that Bid activation was initiated at 9 ± 1 h after UV irradiation, and the average duration of the activation was 75 ± 10 min. Bid activation coincided with a collapse of the mitochondrial membrane potential with an average duration of 50 ± 10 min. When cells were pretreated with Z-IETD-fmk (caspase-8 specific inhibitor) the process of Bid activation was completely inhibited, but the apoptosis was only partially affected. Z-DEVD-fmk (caspase-3 inhibitor) and Z-FA-fmk (non asp specific inhibitor) did not block Bid activation. Furthermore, the endogenous Bid activation with or without Z-IETD-fmk in response to UV irradiation was confirmed by Western blotting. In summary, using the FRET technique, we observed the dynamics of Bid activation during UV-induced apoptosis and found that it was a caspase-8 dependent event.
IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluorescence resonance energy transfer anal. of Bid activation in living cells during UV-induced apoptosis)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 8-7 (Radiation Biochemistry)
IT Lung, neoplasm
(adenocarcinoma; fluorescence resonance energy transfer anal. of Bid activation in living cells during UV-induced apoptosis)
IT 105637-38-5, Z-FA-fmk 179241-78-2, Caspase 8 210344-95-9
210344-98-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluorescence resonance energy transfer anal. of Bid activation in living cells during UV-induced apoptosis)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 10 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1260722 HCAPLUS Full-text
DOCUMENT NUMBER: 147:180751
TITLE: Inducing effects of meisoindigo on apoptosis of leukemia cell line HL-60 and its mechanisms
AUTHOR(S): Wang, Yi; Zhu, Xiaofeng; Xiao, Zhijian; Wang, Honghe; Zhou, Junmin; Mei, Yuping; Deng, Rong; Jiang, Wenqi; Liu, Zongchao
CORPORATE SOURCE: Cancer Center, State Key Laboratory of Oncology in Southern China; Sun Yat-Sen University, Guangzhou, Guangdong Province, 510060, Peop. Rep. China
SOURCE: Aizheng (2005), 24(12), 1464-1468
CODEN: AIZHE4; ISSN: 1000-467X
PUBLISHER: Sun Yat-sen Daxue, Aizheng Zhongxin
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The inducing effects of meisoindigo on apoptosis of myelocytic leukemia cell line HL-60 were investigated to explore the possible mechanisms. After treated by meisoindigo, the proliferation, DNA fragmentation, cellular morphol. and apoptosis of HL-60 cells were detected. The expressions of Fas, Caspase-3, Caspase-8, Caspase-9, poly(ADP-ribose) polymerase (PARP), Bcl-2, Bax and the concentration of cytochrome C were analyzed. Meisoindigo inhibited the proliferation and induced apoptosis in HL-60 cells. When treated with 20 μmol/L meisoindigo for 12-48 h, the proliferation of HL-60 cells was significantly inhibited. When treated for 1 h, the apoptotic rate of HL-60 cells was (3.70±0.56)%; the apoptotic rate was significantly higher in HL-60 cells treated for 3, 6 and 12 h than in the control cells [(19.80±1.13)%, (29.20±2.69)% and (47.05±7.70)% vs. (2.65±0.78)%]. When treated with meisoindigo for 3 h, the typical changes of apoptosis, such as chromatin condensation and DNA ladder, were detected in HL-60 cells. The pos. rate of Fas was significantly higher in cells treated with 20 μmol/L meisoindigo for 1 h than in the control cells [(21.30±1.27)% vs. (9.35±0.21)%]. Meisoindigo activated Caspase-3, Caspase-8, Caspase-9 and PARP, down-regulated the

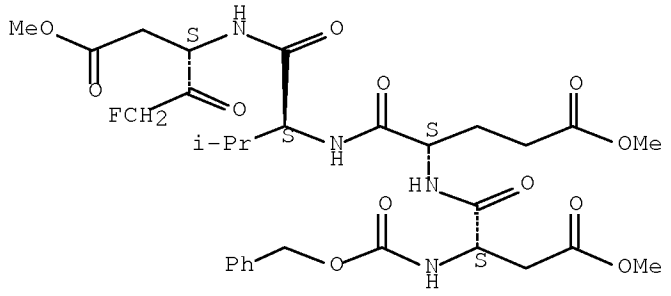
expression of Bcl-2, and up-regulated the expression of Bax and the concentration of cytochrome C. Furthermore, the pretreatment of caspase-3 inhibitor z-DEVD-fmk (N-benzyloxycarbonyl-Asp-Glu-Val-Asp fluoromethylketone) partially reversed the inhibitory effect of meisoindigo on cell proliferation, and decreased apoptosis. When treated with meisoindigo for 5 h, the apoptotic rate was significantly higher in pretreated cells than in cells without pretreatment [(29.8±5.4)% vs. (16.5±5.5)%], when treated with meisoindigo for 12 h, the alive cell number was significantly lower in pretreated cells than in cells without pretreatment [(1.80±0.14)+105/mL vs. (3.57±0.18)+105/mL]. It indicated that meisoindigo could induce apoptosis of HL-60 cells which might relate to regulation of caspases pathway and bcl-2 family proteins.

IT 210344-95-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inducing effects of meisoindigo on apoptosis of leukemia cell line HL-60 and its mechanisms)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

ST meisoindigo leukemia apoptosis caspase signaling bcl2 tumor

IT 97207-47-1, Meisoindigo 210344-95-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inducing effects of meisoindigo on apoptosis of leukemia cell line HL-60 and its mechanisms)

L76 ANSWER 11 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1140680 HCAPLUS Full-text
DOCUMENT NUMBER: 146:59167
TITLE: A missense mutation in Caenorhabditis elegans prohibitin 2 confers an atypical multidrug resistance
AUTHOR(S): Zubovych, Iryna; Doundoulakis, Thomas; Harran, Patrick G.; Roth, Michael G.
CORPORATE SOURCE: Dep. Biochem., Univ. Texas Southwestern Med. Cent., Dallas, TX, 75390-9038, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2006), 103(42), 15523-15528
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hemiasterlin is a potent antimitotic peptide that interferes with microtubule dynamics at picomolar concns. in cell culture. The mol. largely eludes P glycoprotein-mediated drug efflux, and an analog is currently being evaluated in clin. trials as cancer chemotherapy. From a nonclonal genetic screen in Caenorhabditis elegans we isolated eight independent mutants resistant to a synthetic hemiasterlin analog. In one recessive mutant, phb2(ad2154), a point mutation in prohibitin 2 (E130K) protects worms from drug-induced injury. Data indicate that direct binding of hemiasterlin to prohibitin 2 is unlikely. In fact, C. elegans phb2(ad2154) was also found to be resistant to numerous other drugs that bind tubulin and to camptothecin, yet this mutant was sensitive to nocodazole and phalloidin. Thus, prohibitin 2 is implicated in a previously uncharacterized pathway of multidrug resistance.

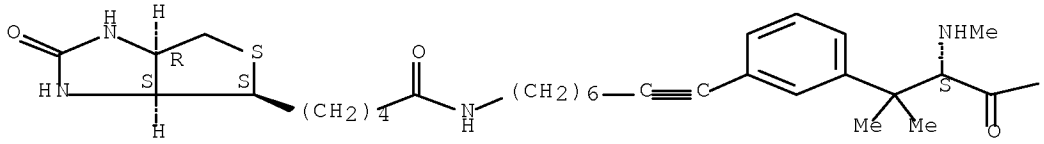
IT 916980-94-4
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(missense mutation in Caenorhabditis elegans prohibitin 2 confers an atypical multidrug resistance)

RN 916980-94-4 HCAPLUS

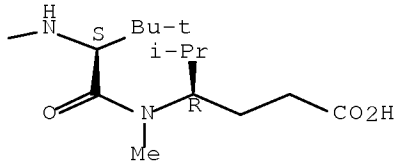
CN L-Valinamide, 3-[8-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-octyn-1-yl]-N,β,β-trimethyl-L-phenylalanyl-N-[(1R)-1-(2-carboxyethyl)-2-methylpropyl]-N,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CC 12-4 (Nonmammalian Biochemistry)
Section cross-reference(s): 3

IT 17466-45-4, Phalloidin 31430-18-9, Nocodazole 157207-90-4, Hemiasterlin 228266-40-8, HTI 286 676632-55-6 916980-93-3 916980-94-4
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(missense mutation in Caenorhabditis elegans prohibitin 2 confers an atypical multidrug resistance)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

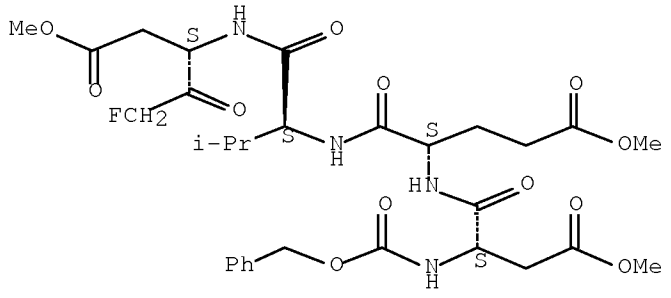
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 12 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:616714 HCAPLUS Full-text
DOCUMENT NUMBER: 145:116941
TITLE: Induction of apoptosis by carbazole alkaloids isolated from Murraya koenigii
AUTHOR(S): Ito, C.; Itoigawa, M.; Nakao, K.; Murata, T.; Tsuboi, M.; Kaneda, N.; Furukawa, H.
CORPORATE SOURCE: Department of Medicinal Chemistry, Faculty of Pharmacy, Meijo University, Nagoya, Japan
SOURCE: Phytomedicine (2006), 13(5), 359-365
CODEN: PYTOEY; ISSN: 0944-7113
PUBLISHER: Elsevier GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the current study, we isolated 10 carbazole alkaloids from the plant species Murraya koenigii (Rutaceae), and examined their effects on the growth of the human leukemia cell line HL-60. Three carbazole alkaloids, mahanine (6), pyrayafoline-D (7) and murrafoline-I (9), showed significant cytotoxicity against HL-60 cells. Fluorescence microscopy with Hoechst 33342 staining revealed that the percentage of apoptotic cells with fragmented nuclei and condensed chromatin was increased in a time-dependent manner after treatment with each alkaloid. Interestingly, each carbazole alkaloid induced the loss of mitochondrial membrane potential. In addition, both caspase-9 and caspase-3 were also time-dependently activated upon treatment with the alkaloids. Caspase-9 and caspase-3 inhibitors suppressed apoptosis induced by these alkaloids. The results suggest that these three alkaloids induced apoptosis in HL-60 cells through activation of the caspase-9/caspase-3 pathway, through mitochondrial dysfunction.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study) (mahanine, pyrayafoline-D and murrafoline-I but not koenine, koenimbine, koenigine, koenidine, mahanimbine, euchrestine-B or mahabinine-A caused mitochondrial dysfunction and membrane potential loss in leukemia cell line HL-60)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
IT Antitumor agents

Cytotoxic agents
Natural products, pharmaceutical
(anti-cancer agents mahanine, pyrayafoline-D and murrafoline-I showed cytotoxic effect by inducing apoptosis through caspase-3/caspase-9 pathway and by mitochondrial dysfunction in human leukemia cell line HL-60)

IT 210344-95-9 210345-04-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mahanine, pyrayafoline-D and murrafoline-I but not koenine, koenimbine, koenigine, koenidine, mahanimbine, euchrestine-B or mahabinine-A caused mitochondrial dysfunction and membrane potential loss in leukemia cell line HL-60)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

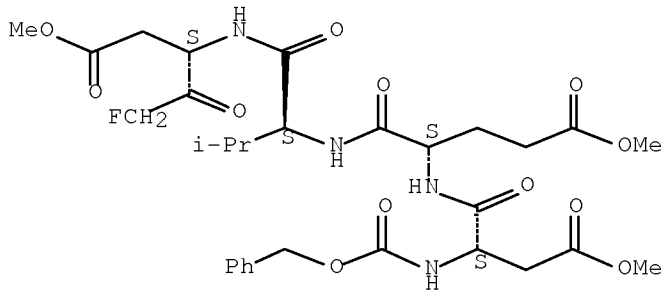
L76 ANSWER 13 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:351252 HCAPLUS Full-text
DOCUMENT NUMBER: 144:403846
TITLE: Caspase-2 activation induced by cisplatin on a human oral squamous cell carcinoma cell line
AUTHOR(S): Fukuchi, Kazuhide; Iseki, Tomio; Morita, Shosuke
CORPORATE SOURCE: Grad. Sch. Dent., Osaka Dental University, Hirakata, 573-1121, Japan
SOURCE: Shika Igaku (2006), 69(1), 23-31
CODEN: SIGAAE; ISSN: 0030-6150
PUBLISHER: Osaka Shika Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Cisplatin (CDDP) is a potent DNA-damaging anticancer agent that induces cytotoxic action by induction of apoptosis. However, its underlying mol. mechanisms remain to be elucidated. We examined the activation of caspase-2, which is involved in the induction of apoptosis by CDDP, in relation to Bax translocation and the interaction of cytochrome c release from mitochondria. The human oral squamous cell carcinoma cell line (HSC-4) was employed in this study. We found that treatment of HSC-4 cells with CDDP decreased cell viability in a dose-dependent manner, and induced apoptosis. One of the apoptosome mols., cytochrome c, was significantly augmented in the cytoplasm by CDDP treatment. Activation of caspase-2, -3, and -9 was detected after treatment with CDDP. Furthermore, apoptosis was blocked when HSC-4 cells that had been treated with CDDP were co-treated with caspase inhibitors such as Z-DEVD-FMK, Z-VDVAD-FMK, and Z-LEHD-AFC. In addition, caspase-2 inhibitor decreased cytochrome c release and delayed Bax translocation into mitochondria. Our results suggest that activation of caspase-2 occurs upstream of the mitochondrial pathway in CDDP-induced apoptosis, and regulates both cytochrome c release and Bax translocation.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)

RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
Section cross-reference(s): 14
ST caspase 2 cisplatin oral squamous cell carcinoma apoptosis
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Organelle
(apoptosome; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Antitumor agents
Apoptosis
Human
Mitochondria
(caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Cytoplasm
(cytosol; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Carcinoma
(oral squamous cell; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Drug interactions
(pharmacokinetic; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT Mouth, neoplasm
(squamous cell carcinoma; caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT 9007-43-6, Cytochrome c, biological studies 169592-56-7, Caspase-3 179241-78-2, Caspase-8 180189-96-2, Caspase-9 182372-14-1, Caspase-2 210344-92-6 210344-95-9 210344-98-2 210345-04-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)
IT 15663-27-1, CDDP
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caspase-2 activation induced by cisplatin on human oral squamous cell carcinoma cell line)

L76 ANSWER 14 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:194165 HCAPLUS Full-text
DOCUMENT NUMBER: 144:254392
TITLE: Preparation of α-keto peptides as calpain inhibitors

INVENTOR(S): Weyermann, Philipp; Von Sprecher, Andreas; Henneboehle, Marco; Herzner, Holger; Lescop, Cyrille; Siendt, Herve
PATENT ASSIGNEE(S): Santhera Pharmaceuticals (Schweiz) GmbH, Switz.
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006021413	A1	20060302	WO 2005-EP9068	20050822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005276635	A1	20060302	AU 2005-276635	20050822
CA 2578006	A1	20060302	CA 2005-2578006	20050822
EP 1791856	A1	20070606	EP 2005-787421	20050822
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008510759	T	20080410	JP 2007-528724	20050822
US 20070293486	A1	20071220	US 2007-574095	20070402

PRIORITY APPLN. INFO.: EP 2004-20190 A 20040825
WO 2005-EP9068 W 20050822
OTHER SOURCE(S): CASREACT 144:254392; MARPAT 144:254392

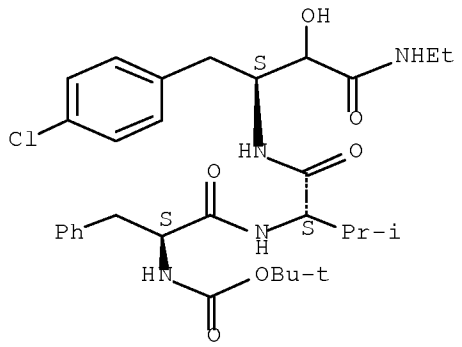
AB The invention relates to novel α-keto carbonyl calpain inhibitors RCH2(CH2)nCONHCHR4CONHCHR3CONHCHR2COCO-X-R1 [R is a ring comprising CH-Y-Z-CH2(CH2)m; Y, Z are independently S, SO or CH2; m, n are 1-6; R1 is H, alkyl, cycloalkyl, aryl, sulfonyl groups, heterocyclyl, carboxy- or carbamoylmethyl or derivs., etc.; X is O or NH; R2, R3 are H, alkyl, cycloalkyl, etc.; R4 is alkyl, cycloalkyl, aryl, etc.] or their pharmaceutically-acceptable salts for the treatment of neurodegenerative and neuromuscular diseases. Disuse atrophy, general muscle wasting, and diseases of the eye can also be treated. The compds. of the invention may also inhibit other thiol proteases such as cathepsin B, cathepsin H, cathepsin L and papain. Multicatalytic Protease also known as proteasome may also be inhibited and the compds. can therefore be used to treat cell proliferative diseases such as cancer, psoriasis, and restenosis. The compds. of the invention are also inhibitors of cell damage by oxidative stress through free radicals and can be used to treat mitochondrial disorders and neurodegenerative diseases, where elevated levels of oxidative stress are involved. They induce the expression of utrophin, which is beneficial for the treatment of Duchenne Muscular Dystrophy and Becker Muscular Dystrophy. Thus, 1,2-dithiolan-3-yl-(CH2)4CO-L-Phe-L-Val-L-p-ClPhe-CONHEt was prepared by condensation of Boc-protected p-chlorophenylalaninal with Et isocyanide, followed by coupling/deprotection reactions, and Dess-Martin oxidation The product showed IC50 = 0.045 μM for inhibition of calpain I.

IT 877465-11-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of α-keto peptides as calpain inhibitors)
RN 877465-11-7 HCAPLUS
CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3-(ethylamino)-2-hydroxy-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63
IT Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiparkinsonian agents
Cataract
Fibroblast
Inflammation
Ischemia
Muscle, disease
Muscular dystrophy
Neoplasm
Neuromuscular diseases
Parkinson's disease
Psoriasis
(preparation of α-keto peptides as calpain inhibitors)
IT 748143-81-9P 877465-11-7P 877465-12-8P 877465-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto peptides as calpain inhibitors)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 15 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:193583 HCAPLUS Full-text
DOCUMENT NUMBER: 144:254390
TITLE: Preparation of α-keto peptides as calpain inhibitors
INVENTOR(S): Weyermann, Philipp; Von Sprecher, Andreas; Henneboehle, Marco; Herzner, Holger; Lescop, Cyrille; Siendt, Herve
PATENT ASSIGNEE(S): Santhera Pharmaceuticals (Schweiz) GmbH, Switz.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006021409	A1	20060302	WO 2005-EP9064	20050822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005276631	A1	20060302	AU 2005-276631	20050822
CA 2577987	A1	20060302	CA 2005-2577987	20050822
EP 1781687	A1	20070509	EP 2005-783059	20050822
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008510756	T	20080410	JP 2007-528720	20050822
US 20080058324	A1	20080306	US 2007-574035	20070402
PRIORITY APPLN. INFO.:			EP 2004-20152 A	20040825
			WO 2005-EP9064 W	20050822

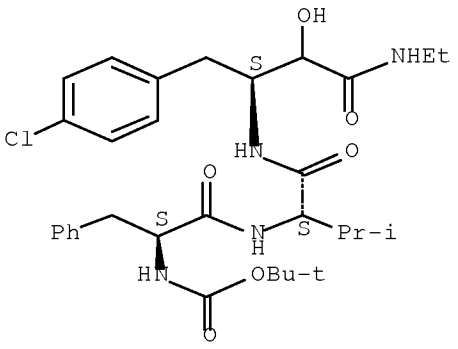
OTHER SOURCE(S): CASREACT 144:254390; MARPAT 144:254390

AB The invention relates to novel α-keto carbonyl calpain inhibitors 2-thienyl-CH2(CH2)1-6CONHCHR4CONHCHR3CONHCHR2COCO-X-R1 [R1 is H, alkyl, cycloalkyl, aryl, sulfonyl groups, heterocyclyl, carboxy- or carbamoylmethyl or derivs., etc.; X is O or NH; R2, R3 are H, alkyl, cycloalkyl, etc.; R4 is alkyl, cycloalkyl, aryl, etc.] or their pharmaceutically-acceptable salts for the treatment of neurodegenerative and neuromuscular diseases. Disuse atrophy, general muscle wasting, and diseases of the eye can also be treated. The compds. of the invention may also inhibit other thiol proteases such as cathepsin B, cathepsin H, cathepsin L and papain. Multicatalytic Protease also known as proteasome may also be inhibited and the compds. can therefore be used to treat cell proliferative diseases such as cancer, psoriasis, and restenosis. The compds. of the invention are also inhibitors of cell damage by oxidative stress through free radicals and can be used to treat mitochondrial disorders and neurodegenerative diseases, where elevated levels of oxidative stress are involved. They induce the expression of utrophin, which is beneficial for the treatment of Duchenne Muscular Dystrophy and Becker Muscular Dystrophy. Thus, 2-thienyl-(CH2)4CO-L-Phe-L-Val-L-p-ClPhe-CONHEt was prepared by condensation of Boc-protected p-chlorophenylalaninal with Et isocyanide, followed by coupling/deprotection reactions, and Dess-Martin oxidation The product showed IC50 = 0.045 μM for inhibition of calpain I.

IT 877465-11-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto peptides as calpain inhibitors)

RN 877465-11-7 HCAPLUS
CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3-(ethylamino)-2-hydroxy-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63
IT Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiparkinsonian agents
Cataract
Fibroblast
Inflammation
Ischemia
Muscle, disease
Muscular dystrophy
Neoplasm
Neuromuscular diseases
Parkinson's disease
Psoriasis
(preparation of α-keto peptides as calpain inhibitors)
IT 748143-81-9P 877465-11-7P 877465-12-8P 877466-31-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto peptides as calpain inhibitors)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 16 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:78830 HCAPLUS Full-text
DOCUMENT NUMBER: 145:433
TITLE: A comparison of the signal pathways between the TNFα- and oridonin-induced murine L929 fibrosarcoma cell death
AUTHOR(S): Huang, Jian; Wu, Lijun; Tashiro, Shin-ichi; Onodera, Satoshi; Ikejima, Takashi
CORPORATE SOURCE: China-Japan Research Institute of Medical and Pharmaceutical Sciences, Department of Phytochemistry, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Acta Medica Okayama (2005), 59(6), 261-270
CODEN: AMOKAG; ISSN: 0386-300X
PUBLISHER: Okayama University Medical School
DOCUMENT TYPE: Journal
LANGUAGE: English

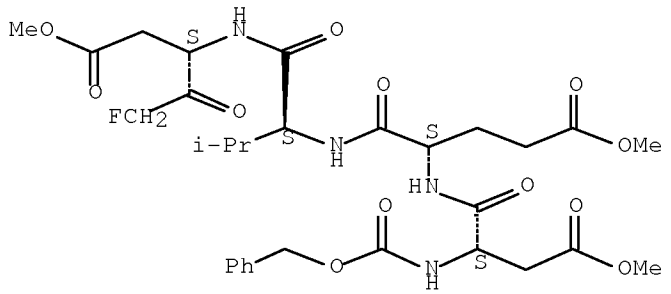
AB Oridonin, an active component isolated from Rabdosia rubescences, has been reported to have antitumor effects. In this study, we compared the signal transduction pathways between TNFα- and oridonin-induced L929 cell death. Oridonin and TNFα initiated apoptotic morphol. changes, but DNA fragmentation was found in TNFα-treated L929 cells but not in oridonin-treated ones. The pan-caspase inhibitor (z-VAD-fmk), caspase-8 inhibitor (z-IETD-fmk) and caspase-3 inhibitor (z-DEVD-fmk) augmented oridonin- and TNFα-induced cell death. However, the caspase-9 inhibitor (z-LEHD-fmk) only increased oridonin-induced L929 cell death. Moreover, poly (ADP-ribose) polymerase (PARP) was cleaved in oridonin-treated L929 cells but not in the TNFα-treated groups, and the caspase-3 inhibitor (z-DEVD-fmk) failed to inhibit PARP cleavage. These results showed that only oridonin-induced L929 cell death required PARP degradation in a caspase-3 independent manner. In addition, oridonin increased the ratio of Bax/Bcl-2 protein expression, but TNFα did not. TNFα induced p38 and ERK activation, whereas oridonin triggered only ERK activation. We also investigated the effect of oridonin on intracellular TNFα expression, and found that oridonin augmented endogenous pro-TNFα expression and its upstream protein IκB phosphorylation. These results indicated that although oridonin promoted endogenous pro-TNFα expression, a great difference existed between the signal pathways through which TNFα- and oridonin-induced cell death.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor necrosis factor-α and oridonin dose-dependently induced cell death with differential involvement of signaling pathways including caspases, PARP, Bax/Bcl-2 protein expression and MAPK modulation in murine L929 fibrosarcoma cells)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

ST cell death tumor necrosis factor alpha fibrosarcoma apoptosis oridonin

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IκB (inhibitor of NF-κB); oridonin promoted endogenous pro-tumor necrosis factor-α expression by reduced IκB expression and increased IκB phosphorylation in murine L929 fibrosarcoma cells)

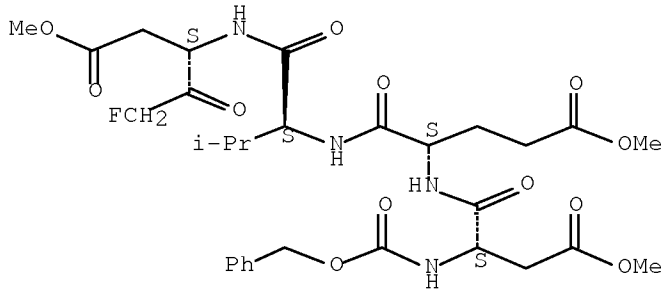
IT Signal transduction, biological
(MAPK cascades, ERK was involved in both tumor necrosis factor-α and oridonin induced cell death in murine L929 fibrosarcoma cells)
IT Sarcoma
(fibrosarcoma; tumor necrosis factor-α and oridonin induced cell death with differential involvement of signaling pathways including caspases, PARP, Bax/Bcl-2 protein expression and MAPK modulation in murine L929 fibrosarcoma cells)
IT Antitumor agents
(oridonin with anti-tumor effect induced cell death, which was regulated by caspase-3, -8 and PARP, increased ratio of Bax/Bcl-2 protein expression and ERK activation in murine L929 fibrosarcoma cells)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p38; MAPK cascades, p38 was involved in tumor necrosis factor-α induced cell death but not in oridonin induced cell death in murine L929 fibrosarcoma cells)
IT Apoptosis
(tumor necrosis factor-α and oridonin dose dependently induced apoptosis in murine L929 fibrosarcoma cells)
IT Cell death
(tumor necrosis factor-α and oridonin dose-dependently induced cell death with differential involvement of signaling pathways including caspases, PARP, Bax/Bcl-2 protein expression and MAPK modulation in murine L929 fibrosarcoma cells)
IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor necrosis factor-α induced cell death was regulated by caspase-3, -8 and -9, p38, ERK and oridonin promoted endogenous pro-tumor necrosis factor-α expression in murine L929 fibrosarcoma cells)
IT 142243-02-5, MAPK
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAPK cascades, ERK was involved in both tumor necrosis factor-α and oridonin induced cell death but p38 was involved only in tumor necrosis factor-α induced cell death in murine L929 fibrosarcoma cells)
IT 169592-56-7, Caspase 3 179241-78-2, Caspase 8 180189-96-2, Caspase 9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3, -8 and -9 were differentially involved in tumor necrosis factor-α and oridonin induced cell death in murine L929 fibrosarcoma cells)
IT 9055-67-8, Poly (ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(poly (ADP-ribose) polymerase was cleaved in oridonin induced cell death but not in oridonin tumor necrosis factor-α induced cell death in murine L929 fibrosarcoma cells)
IT 187389-52-2 210344-95-9 210344-98-2 210345-04-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor necrosis factor-α and oridonin dose-dependently induced cell death with differential involvement of signaling pathways including caspases, PARP, Bax/Bcl-2 protein expression and MAPK modulation in murine L929 fibrosarcoma cells)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 17 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1317136 HCAPLUS Full-text
DOCUMENT NUMBER: 144:480497
TITLE: Apoptotic pathway of norcantharidin-induced HeLa cells apoptosis
AUTHOR(S): An, Weiwei; Wang, Minwei; Gong, Xianfeng; Tashiro, Shinichi; Ododera, Satoshi; Ikejima, Takashi
CORPORATE SOURCE: China-Japan Research Institute of Medical and Pharmaceutical Sciences, Shenyang Pharmaceutical University, Shenyang, Liaoning Province, 110016, Peop. Rep. China
SOURCE: Zhongguo Bingli Shengli Zazhi (2005), 21(3), 417-421
CODEN: ZBSZEB; ISSN: 1000-4718
PUBLISHER: Jinan Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The apoptotic pathway of norcantharidin (NCTD)-induced HeLa cells death was examined NCTD induced HeLa cells apoptosis and the apoptosis was partially reversed by the inhibitors of caspase -family (-3, -8, -10). The activities of caspase -3, -8 and -9 were significantly increased after treated with NCTD. The expression of the inhibitor of caspase-3 activated DNase (ICAD) was decreased in a time dependent manner. NCTD induces HeLa cells apoptosis through activating caspase pathways.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(apoptotic pathway of norcantharidin-induced HeLa cells apoptosis)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
ST norcantharidin apoptosis pathway antitumor cervix carcinoma caspase
IT Uterus, neoplasm
(cervix, carcinoma; apoptotic pathway of norcantharidin-induced HeLa cells apoptosis)
IT Carcinoma
Uterus
(cervix; apoptotic pathway of norcantharidin-induced HeLa cells apoptosis)
IT 169592-56-7, Caspase 3 179241-78-2, Caspase 8 180189-96-2, Caspase 9 187389-52-2 210344-95-9 210344-98-2 253186-30-0

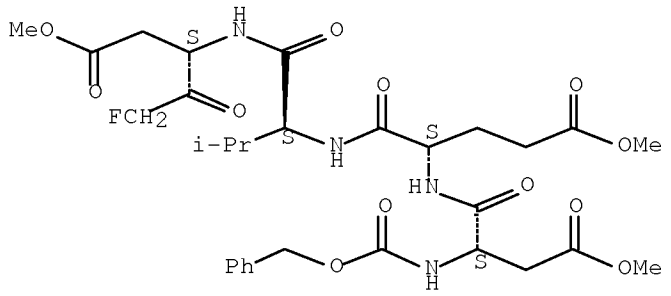
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(apoptotic pathway of norcantharidin-induced HeLa cells apoptosis)

L76 ANSWER 18 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1308948 HCAPLUS Full-text
DOCUMENT NUMBER: 144:324306
TITLE: Contribution of reactive oxygen species and caspase-3 to apoptosis and attenuated ICAM-1 expression by paclitaxel-treated MDA-MB-435 breast carcinoma cells
AUTHOR(S): Fawcett, Helen; Mader, Jamie S.; Robichaud, Matthew; Giacomantonio, Carman; Hoskin, David W.
CORPORATE SOURCE: Departments of Microbiology & Immunology, Faculty of Medicine, Dalhousie University, Halifax, NS, B3H 1X5, Can.
SOURCE: International Journal of Oncology (2005), 27(6), 1717-1726
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Paclitaxel is a microtubule-stabilizing and apoptosis-inducing drug that is commonly used to treat metastatic breast cancer, although the mechanism of paclitaxel-induced apoptosis remains incompletely understood. Furthermore, adhesion mol. expression is attenuated on mouse mastocytoma and human leukemia cells that survive short-term culture in the presence of paclitaxel. In the present study we show that MDA-MB-435 human breast carcinoma cells that survived culture for 72 h in the presence of submaximal cytotoxic concns. of paclitaxel (0.02 and 0.01 μg/mL) showed decreased expression of the adhesion mol. ICAM-1. Paclitaxel treatment of MDA-MB-435 cells was associated with the generation of reactive oxygen species (ROS), dissipation of mitochondrial transmembrane potential, and the activation of caspase-3. The antioxidant glutathione protected MDA-MB-435 cells from paclitaxel-induced cytotoxicity and reduced ICAM-1 expression. In addition, a selective inhibitor of caspase-3 (Z-DEVD-FMK), as well as a pan-caspase inhibitor (Z-VAD-FMK), partially prevented the decrease in ICAM-1 expression observed following paclitaxel treatment, but did not protect against paclitaxel-induced cytotoxicity. We conclude that the paclitaxel-induced reduction in ICAM-1 expression by MDA-MB-435 breast carcinoma cells is both ROS- and caspase-dependent, whereas paclitaxel-induced cytotoxicity is ROS-dependent and does not involve caspases. Decreased ICAM-1 expression by breast carcinoma cells that survive paclitaxel treatment may neg. impact on cytotoxic lymphocyte-mediated destruction of paclitaxel-resistant breast cancer cells in the context of chemo-immunotherapy or chemo-adoptive immunotherapy.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
ST paclitaxel breast carcinoma ICAM 1 apoptosis caspase 3 antitumor
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD54; paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1); paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT Mammary gland, neoplasm
(carcinoma; paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT Carcinoma
(mammary; paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT Apoptosis
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced apoptosis was only ROS-dependent)
IT Antitumor agents
Cytotoxic agents
Human
Mammary gland
Mitochondrial membrane potential
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)
IT 7782-44-7D, Oxygen, reactive species 169592-56-7, Caspase-3

187389-52-2 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)

IT 33069-62-4, Paclitaxel
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paclitaxel-induced decrease in ICAM-1 by human breast carcinoma cell MDA-MB-435 was associated with ROS activation, mitochondrial transmembrane potential and caspase-3 but paclitaxel-induced cytotoxicity was only ROS-dependent)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

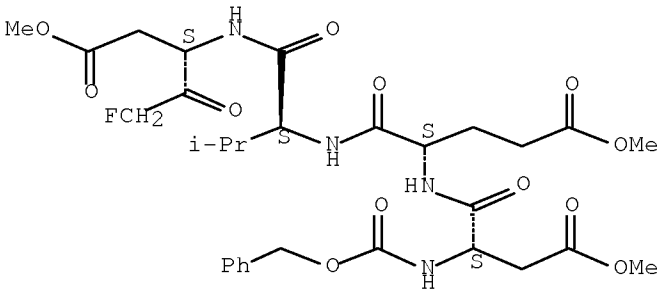
L76 ANSWER 19 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1291580 HCAPLUS Full-text
DOCUMENT NUMBER: 144:285731
TITLE: Modes of action of alpha-hederin and thymoquinone, active constituents of Nigella sativa, Against HEp-2 cancer cells
AUTHOR(S): Rooney, Sara; Ryan, M. F.
CORPORATE SOURCE: Department of Zoology, University College Dublin, Belfield, Dublin, Ire.
SOURCE: Anticancer Research (2005), 25(6B), 4255-4259
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Our previous studies on active constituents of Nigella sativa have indicated that cell death induced by thymoquinone and alpha-hederin was dose- and time-dependent, in a range of four cancer cell lines. Both compds. elicited necrosis and apoptosis with a higher incidence of the latter induced by thymoquinone. As HEp-2 human laryngeal carcinoma cells were the most susceptible, we sought to better understand the mechanisms involved by using buthionine sulfoximine (BSO), a selective inhibitor of glutathione (GSH) synthesis, to determine the importance of GSH in the apoptosis elicited, using cisplatin as internal standard BSO significantly enhanced alpha-hederin- and cisplatin- mediated toxicity as assessed by the MTT assay, without changes in apoptosis or necrosis levels. Although the MTT assay did not indicate BSO potentiation of thymoquinone, apoptosis levels were significantly enhanced following this combination, without changes in necrosis. Thymoquinone and cisplatin significantly decreased GSH levels in a dose-dependent manner, with BSO pre-treatment synergistically depleting GSH levels in only thymoquinone-treated cells. As the caspase 3 inhibitor, Z-DEVD-fmk significantly decreased thymoquinone- and cisplatin-induced apoptosis, GSH depletion and caspase 3-activation mediate thymoquinone-induced apoptosis, in this cell line.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(active constituent of Nigella sativa thymoquinone depleted GSH and induced apoptosis in HEp-2 cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation mediate Tq induced apoptosis)

RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.

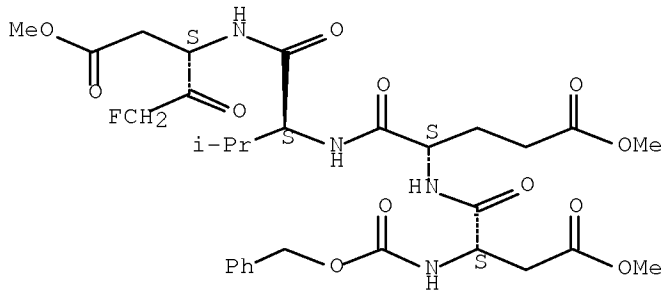


CC 1-6 (Pharmacology)
ST Nigella thymoquinone alpha hederin buthionine sulfoximine laryngeal carcinoma apoptosis
IT Necrosis
(active constituent of Nigella sativa thymoquinone and alpha-hederin did not induced necrosis significantly in HEp-2 laryngeal carcinoma cell line)
IT Nigella sativa
(active constituent of Nigella sativa thymoquinone but not alpha-hederin depleted GSH and induced apoptosis in HEp-2 laryngeal carcinoma cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk)
IT Larynx, neoplasm
(carcinoma; active constituent of Nigella sativa thymoquinone depleted GSH and induced apoptosis in HEp-2 cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation mediate Tq induced apoptosis)
IT Carcinoma
(laryngeal; active constituent of Nigella sativa thymoquinone depleted GSH and induced apoptosis in HEp-2 cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation mediate Tq induced apoptosis)
IT Apoptosis
(thymoquinone and BSA depleted GSH and induced apoptosis in HEp-2 laryngeal carcinoma cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation mediate Tq induced apoptosis)
IT 27013-91-8, α-Hederin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(active constituent of Nigella sativa alpha-hederin did not depleted GSH and induced apoptosis in HEp-2 laryngeal carcinoma cell line)
IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(active constituent of Nigella sativa thymoquinone depleted GSH and induced apoptosis in HEp-2 cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation mediate Tq induced apoptosis)
IT 169592-56-7, Caspase-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymoquinone and BSA depleted GSH and induced apoptosis in HEp-2 laryngeal carcinoma cell line while was reversed by caspase 3 inhibitor Z-DEVD-fmk suggesting GSH depletion, caspase 3 activation

mediate Tq induced apoptosis)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 20 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:844742 HCAPLUS Full-text
DOCUMENT NUMBER: 143:222420
TITLE: Effects of antioxidants and caspase-3 inhibitor on the phenylethyl isothiocyanate-induced apoptotic signaling pathways in human PLC/PRF/5 cells
AUTHOR(S): Wu, Shu-Jing; Ng, Lean Teik; Lin, Chun-Ching
CORPORATE SOURCE: Graduate Institute of Natural products, College of Pharmacy, Kaohsiung Medical University, Kaohsiung, 807, Taiwan
SOURCE: European Journal of Pharmacology (2005), 518(2-3), 96-106
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phenylethyl isothiocyanate (PEITC) is a well recognized potential chemopreventive compound against human cancers. In this study, the mol. mechanism of PEITC-induced apoptosis was examined with two antioxidants (N-acetyl-cysteine and vitamin E) and a caspase-3 inhibitor (z-DEVD-fmk). Results demonstrated that PEITC significantly induced human hepatoma PLC/PRF/5 (CD95-neg.) cells undergoing apoptosis. Treatment with 0.apprx.10 μM PEITC-triggered cell apoptosis as revealed by the externalization of annexin V-targeted phosphatidylserine and the subsequent appearance of sub-G1 population. Results also displayed that PEITC-induced apoptosis involves the up-regulation of p53 and Bax protein, down-regulation of the XIAP, Bcl-2, Bcl-XL and Mcl-1 proteins, cleavage of Bid, and the release of cytochrome c and Smac/Diablo, which were accompanied by the activation of caspases -9, -3 and -8. PEITC-induced the generation of reactive oxygen species and the decrease of mitochondrial membrane potential ($\Delta\psi m$) in a time-dependent pattern. N-acetyl-cysteine and vitamin E at 100 μM, and z-DEVD-fmk at 50 μM markedly blocked PEITC-induced apoptosis, which was demonstrated by a decline in the reactive oxygen species generation and the release of the cytochrome c and Smac/Diablo from mitochondria to the cytosol. N-acetyl-cysteine, vitamin E and z-DEVD-fmk also prevented the PEITC in inducing the loss of $\Delta\psi m$. They also affected the activity of XIAP and Bax proteins. Taken together, these studies suggest that PEITC is an apoptotic inducer that acts on the mitochondria and the feedback amplification loop of caspase-8/Bid pathways in PLC/PRF/5 cells.
IT 210344-95-9
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of antioxidants and caspase-3 inhibitor on the phenylethyl isothiocyanate-induced apoptotic signaling pathways in human PLC/PRF/5 cells)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



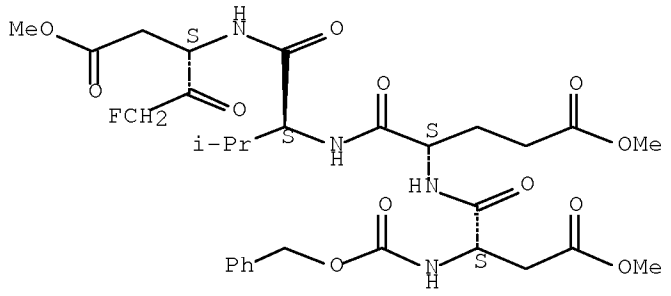
CC 1-12 (Pharmacology)
IT 616-91-1, N-Acetyl-cysteine 1406-18-4, Vitamin E 2257-09-2, Phenylethyl isothiocyanate 210344-95-9
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of antioxidants and caspase-3 inhibitor on the phenylethyl isothiocyanate-induced apoptotic signaling pathways in human PLC/PRF/5 cells)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 21 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:509698 HCAPLUS Full-text
DOCUMENT NUMBER: 143:278551
TITLE: Inhibition of cell growth and induction of apoptosis in human prostate cancer cell lines by 6-aminoquinolone WM13
AUTHOR(S): Minelli, Alba; Bellezza, Ilaria; Siciliano, Emanuela; Liguori, Lavinia; Tabarrini, Oriana; Cecchetti, Violetta; Fravolini, Arnaldo
CORPORATE SOURCE: Dipartimento di Scienze Biochimiche e Biotecnologie Molecolari, Sezione di Biochimica Cellulare, Universita di Perugia, Perugia, 06123, Italy
SOURCE: Oncology Reports (2005), 13(6), 1113-1120
CODEN: OCRPEW; ISSN: 1021-335X
PUBLISHER: Oncology Reports
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluoroquinolones affect the proliferation and apoptotic cell death of several human malignancies. Therefore, we investigated whether new 6-aminoquinolone derivs., initially synthesized as anti-HIV agents, could affect the proliferation and apoptotic cell death of human prostate cancer cell lines. PC3 and LNCaP cell lines were used as models of androgen-resistant and androgen-responsive prostate cancer, and proliferation of PC3 and LNCaP cells was strongly inhibited by 6-aminoquinolone WM13. Cytotoxicity, which was more pronounced in LNCaP, was accompanied by morphol. changes, DNA damage, arrest at the S/G2/M phase of the cell cycle, and an increase of the sub-G1 population. Mol. mechanism underlying WM13-induced cell death involved caspase-8 and -3 and modulation of the expression of apoptotic genes, as well as cleavage of poly-ADP ribose polymerase. Cell death following the treatment of human prostate cancer cell lines with WM13 can be attributed to apoptosis which, depending on the cell line, proceeds through different pathways.
IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of cell growth and induction of apoptosis in human prostate cancer cell lines by 6-aminoquinolone WM13)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

ST aminoquinolone prostate cancer cell proliferation antitumor

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through Bax proteins)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through Bcl-2 protein)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-repairing; WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through cleavage of DNA repair enzyme poly-ADP ribose polymerase)

IT DNA damage
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation accompanied by DNA damage evident by cleavage of DNA repair enzyme poly-ADP ribose polymerase)

IT Cell cycle
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation accompanied by cell cycle arrest at S/G2/M phase and increase of sub-G1 population)

IT Apoptosis
Cell proliferation
Human
Prostate gland, neoplasm
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through caspase-8, -3, Bax, Bcl-2 proteins and cleavage of poly-ADP ribose polymerase)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p21CIP1; WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation accompanied by cell cycle arrest at

S/G2/M phase and increase of sub-G1 population)
IT 791812-49-2
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6-aminoquinolone WM13 strongly inhibited prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through caspase-8, -3, Bax, Bcl-2 proteins and cleavage of poly-ADP ribose polymerase)
IT 791812-57-2
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6-aminoquinolone WM16 exhibited slight inhibition of human prostate cancer cell line PC3, LNCaP proliferation)
IT 791812-53-8
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6-aminoquinolone WM20 exhibited slight inhibition of human prostate cancer cell line PC3, LNCaP proliferation)
IT 169592-56-7, Caspase-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through caspase-3)
IT 179241-78-2, Caspase-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through caspase-8 protein)
IT 9055-67-8, Poly-ADP ribose polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(WM13 strongly inhibited human prostate cancer cell line PC3, LNCaP proliferation with pronounced cytotoxicity in LNCaP through cleavage of DNA repair enzyme poly-ADP ribose polymerase)
IT 187389-52-2 210344-95-9 210344-98-2 210345-04-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of cell growth and induction of apoptosis in human prostate cancer cell lines by 6-aminoquinolone WM13)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 22 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:366657 HCAPLUS Full-text
DOCUMENT NUMBER: 143:126016
TITLE: Pycnogenol induces differentiation and apoptosis in human promyeloid leukemia HL-60 cells
AUTHOR(S): Huang, W. W.; Yang, J. S.; Lin, C. F.; Ho, W. J.; Lee, M. R.
CORPORATE SOURCE: Department of Biology, China Medical University, Taichung, Taichung, 404, Taiwan
SOURCE: Leukemia Research (2005), 29(6), 685-692
CODEN: LEREDD; ISSN: 0145-2126
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pycnogenol, rich of many phytochems. of medical value, is a commercialized nutrient supplement extracted from the bark of European coastal pine. In this study, we investigated the anti-tumor effects of Pycnogenol on HL-60, U937 and K562 human leukemia cell lines. We found that Pycnogenol inhibited cell proliferation dose- and time-dependently, and the IC50s of Pycnogenol on HL-60, U937 and K562 cells were 150, 40 and 100 μg/mL, resp. When HL-60 cells

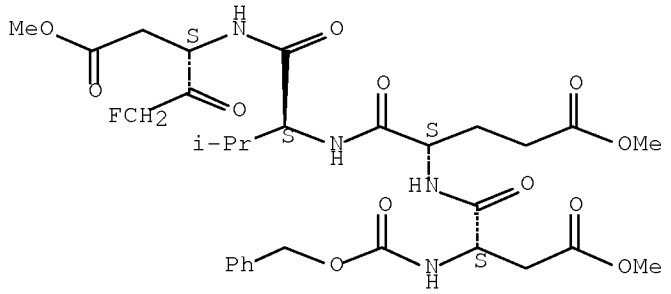
were incubated with low concns. of Pycnogenol (50, 100 and 125 μg/mL) for 24 h, a prominent G0/G1 arrest was observed, followed by gradual accumulation of sub-G0/G1 nuclei. At 48 h of treatment, 50-70% of HL-60 cells differentiated, as evidenced by morphol. changes, NBT reduction, induction of NSE activity, and increases of cell surface expression of CD11b. However, results from Annexin V/PI staining, DAPI staining and DNA fragmentation assay indicated that Pycnogenol induced HL-60, U937 and K562 cell apoptosis at their resp. IC50s after 24 h of treatments. Pretreatment of z-DEVD-fmk, a caspase-3 specific inhibitor, not only decreased caspase-3 activity but also reduced the percentage of apoptotic cells induced by Pycnogenol. This indicated that caspase-3 activation was involved in Pycnogenol induced-apoptosis. In conclusion, Pycnogenol induced differentiation and apoptosis in leukemia cells. Our data suggest that Pycnogenol could serve as a potent cancer chemopreventive or chemotherapeutic agent for human leukemia.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pycnogenol induced apoptosis mediated by activation of caspase-3 in human leukemia HL-60, U937 and K562 cell lines)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

IT 169592-56-7, Caspase-3 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pycnogenol induced apoptosis mediated by activation of caspase-3 in human leukemia HL-60, U937 and K562 cell lines)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 23 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:342125 HCAPLUS Full-text

DOCUMENT NUMBER: 142:456481

TITLE: Potential mechanism of phytochemical-induced apoptosis in human prostate adenocarcinoma cells: Therapeutic synergy in genistein and β-lapachone combination treatment

AUTHOR(S): Kumi-Diaka, James; Saddler-Shawnette, Simone; Aller, Alex; Brown, Jayann

CORPORATE SOURCE: Department of Biological Sciences, Schmidt College of Science, Florida Atlantic University, Davie, FL, 33314, USA

SOURCE: Cancer Cell International (2004), 4, No pp. given
CODEN: CCIACC; ISSN: 1475-2867
URL: http://www.cancerci.com/content/pdf/1475-2867-4-5.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

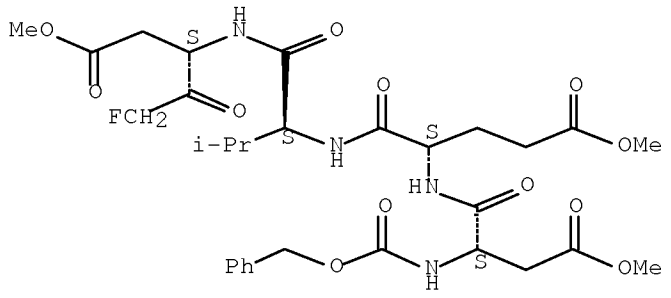
AB Background: Prostate cancer is the second leading cause of male death in the United States. The incidence increases most rapidly with age, and multiple genetic and epigenetic factors have been implicated in the initiation, progression, and metastasis of the cancer. Nevertheless, scientific knowledge of the mol. mechanisms underlying the disease is still limited; and hence treatment has only been partially successful. The objective of the current studies was to examine the role of caspase 3 (CPP32) and NAD(P)H:quinone oxidoreductase (NQOI) in the signaling of genistein-and β-lapachone (bLap)-induced apoptosis in human prostate carcinoma cells PC3. Results: Both genistein and bLap produced dose-dependent growth inhibition and treatment-induced apoptosis in PC3. Treatment with caspase 3 inhibitor, DEVD-fmk before exposure to genistein, significantly inhibited caspase 3 expression and treatment-induced apoptosis; implicating CPP32 as the main target in genistein-induced apoptosis in PC3. Contrary to this observation, inhibition of CPP32 did not significantly influence bLap-induced apoptosis; implying that the major target of bLap-induced apoptosis may not be the caspase. Treatment with NQOI inhibitor, dicoumarol (50 μM), prior to exposure of PC3 to bLap led to significant decrease in bLap toxicity concurrent with significant decrease in treatment-induced apoptosis; thus implicating NQOI as the major target in β-lapachone-induced apoptosis in PC3. In addition, the data demonstrated that NQOI is the major target in bLap-genistein (combination)-induced apoptosis. On the contrary, blocking NQOI activity did not significantly affect genistein-induced apoptosis; implying that NQOI pathway may not be the main target for genistein-induced apoptosis in PC3 cells. Furthermore, blocking NQOI and CPP32 did not confer 100% protection against genistein-induced or bLap-induced apoptosis. Conclusion: The data thus demonstrate that both genistein-and bLap-induced apoptosis are mostly but not completely dependent on CPP32 and NQOI resp. Other minor alternate death pathways may be involved. This suggests that some death receptor signals do not utilize the caspase CPP32 and/or the NQOI death pathways in PC3. The demonstrated synergism between genistein and bLap justifies consideration of these phytochems. in chemotherapeutic strategic planning.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prior treatment with caspase 3 inhibitor DEVD-fmk inhibited caspase 3 expression and genistein treatment-induced apoptosis in PC3 human prostate adenocarcinoma cell line indicating CPP32 as main target in genistein-induced apoptosis)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

IT Prostate gland, neoplasm
(carcinoma; genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein + bLap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT Apoptosis
Human
(genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein + bLap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT Antitumor agents
Combination chemotherapy
(genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein b + Lap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT Cell proliferation
(inhibition; genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein + bLap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT Carcinoma
(prostatic; genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein + bLap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT Drug interactions
(synergistic; genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein b + Lap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

IT 446-72-0, Genistein 4707-32-8, β-Lapachone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genistein with bLap showed dose-dependent growth inhibition, induced apoptosis and major target for bLap-, genistein + bLap-induced apoptosis appear to be NQOI, genistein-induced apoptosis to be CPP32 in human prostate cancer cell line PC3)

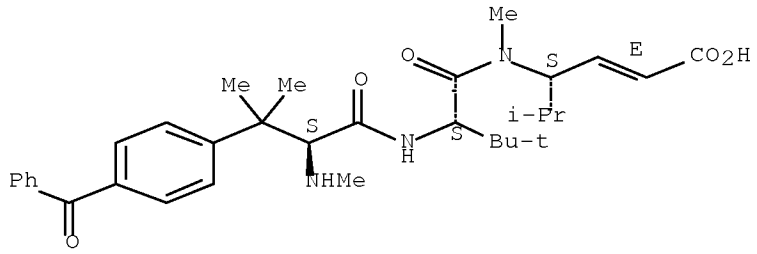
IT 169592-56-7, Caspase 3 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prior treatment with caspase 3 inhibitor DEVD-fmk inhibited caspase 3 expression and genistein treatment-induced apoptosis in PC3 human prostate adenocarcinoma cell line indicating CPP32 as main target in

genistein-induced apoptosis)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 24 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:312854 HCAPLUS Full-text
DOCUMENT NUMBER: 143:21680
TITLE: Two Photoaffinity Analogues of the Tripeptide, Hemiasterlin, Exclusively Label α-Tubulin
AUTHOR(S): Nunes, Maria; Kaplan, Joshua; Wooters, Joseph; Hari, Malathi; Minnick, Albert A., Jr.; May, Michael K.; Shi, Celine; Musto, Sylvia; Beyer, Carl; Krishnamurthy, Girija; Qiu, Yongchang; Loganzo, Frank; Ayral-Kaloustian, Semiramis; Zask, Arie; Greenberger, Lee M.
CORPORATE SOURCE: Oncology Research, Chemical and Screening Sciences, Radiosynthesis Group, and Bioorganic Enzymology, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Biochemistry (2005), 44(18), 6844-6857
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A synthetic analog of the tripeptide hemiasterlin, designated HTI-286, depolymerizes microtubules, is a poor substrate for P-glycoprotein, and inhibits the growth of paclitaxel-resistant tumors in xenograft models. Two radiolabeled photoaffinity analogs of HTI-286, designated 4-benzoyl-N,β,β-trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide (probe 1) and N,β,β-trimethyl-L-phenylalanyl-4-benzoyl-N-[(1S,2E)-3-carboxy-1- isopropyl-2-butenyl]-N,β,β-trimethyl-L-phenylalaninamide (probe 2), were made to help identify HTI-286 binding sites in tubulin. HTI-286, probe 1, and probe 2 had similar affinities for purified tubulin [apparent KD(app) = 0.2-1.1 μM], inhibited polymerization of purified tubulin .apprx.80%, and were potent inhibitors of cell growth (IC50 = 1.0-22 nM). Both radiolabeled probes labeled exclusively α-tubulin. Labeling by [3H]probe 1 was inhibited by probe 1, HTI-286, vinblastine, or dolastatin 10 (another peptide antimitotic agent that depolymerizes microtubules) but was either unaffected or enhanced (at certain temps.) by colchicine or paclitaxel. [3H]Probe 1 also labeled exclusively tubulin in cytosolic exts. of whole cells. [3H]Probe 1 also labeled exclusively tubulin in cytosolic exts. of whole cells. The major, if not exclusive, contact site for probe 1 was mapped to residues 314-339 of α-tubulin and corresponds to the sheet 8 and helix 10 region. This region is known to (1) have longitudinal interactions with β-tubulin across the interdimer interface, (2) have lateral interactions with adjacent protofilaments, and (3) contact the N-terminal region of stathmin, a protein that induces depolymn. of tubulin. Binding of probe 1 to this region may alter the conformation of tubulin outside the labeling domain, since enzymic removal of the C-terminus of only α-tubulin by subtilisin after, but not before, photolabeling is blocked by probe 1. These results suggest that hemiasterlin is in close contact with α-tubulin and may span the interdimer interface so that it contacts the vinblastine- and dolastatin 10-binding sites believed to be in β-tubulin. In addition, we speculate that antimitotic peptides mimic the interaction of stathmin with tubulin.
IT 853013-41-9
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(two photoaffinity analogs of tripeptide, hemiasterlin, exclusively

label α-tubulin)
RN 853013-41-9 HCAPLUS
CN L-Valinamide, 4-benzoyl-N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-propenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 6-3 (General Biochemistry)
Section cross-reference(s): 9
IT 228266-40-8, HTI-286 676634-31-4 853013-41-9
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(two photoaffinity analogs of tripeptide, hemiasterlin, exclusively label α-tubulin)
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 25 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:312492 HCAPLUS Full-text
DOCUMENT NUMBER: 142:441449
TITLE: Phosphorylated and hypoacetylated mutant p53 enhances cisplatin-induced apoptosis through caspase-9 pathway in the absence of transcriptional activation or translation
AUTHOR(S): Lai, Ming-Derg; Lin, Wan-Chi; Sun, Yih-Min; Chang, Fu-Lin
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, National Cheng Kung University, Tainan, 701, Taiwan
SOURCE: International Journal of Molecular Medicine (2005), 15(4), 725-734
CODEN: IJMMFG; ISSN: 1107-3756
PUBLISHER: International Journal of Molecular Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It is not completely understood how certain epithelial cells harboring mutant p53 have better response to chemotherapy. We investigate the mechanism of cisplatin-induced apoptosis in two resistant cell lines (parental TCCSUP and R273L mutant p53 transfectant) and two sensitive cell lines (V143A and N247I mutant p53 transfectants). Activation of caspase 9 was demonstrated by Western blotting, and specific inhibitor for caspase 9 could inhibit apoptosis. Inhibitors for caspases 1, 2, 6, and 8 had no effect on apoptosis. Transcriptional repression of Bcl-2 occurred during apoptosis and could be reversed by the treatment of histone deacetylase inhibitor trichostatin A (TSA). The expression of Noxa, p53 inducible ribonucleotide reductase subunit

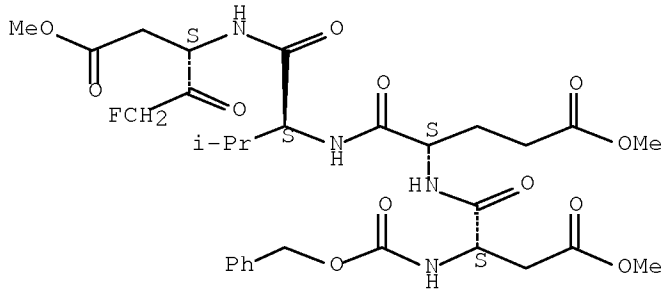
2 (p53R2), and p53 inducible death domain (PIDD) gene were not elevated with treatment of cisplatin (CDDP). Surface trafficking of Fas or Fas-L was not observed Ser15 of wild-type p53 and mutant p53 was phosphorylated in response to cisplatin. Acetylation of wild-type p53 increased, while acetylation of mutant p53 decreased during cisplatin treatment. Both transcriptional inhibitor actinomycin D and translational inhibitor cycloheximide did not inhibit apoptosis. These results indicated that phosphorylated and hypoacetylated mutant p53 could enhance cisplatin-induced apoptosis through activation of caspase 9 independent of transcriptional activation and translation.

IT 210344-95-9, z-DEVD-fmk
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylated, hypoacetylated mutant p53 raised cisplatin-induced apoptosis by activating caspase-9 independent of transcription activation, translation in bladder cancer cells TCCSUP-143-4, TCCSUP-247-5 but not in TCCSUP, TCCSUP-273-6)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

ST cisplatin apoptosis caspase transcription activation translation bladder cancer antitumor

IT Antitumor agents
Bladder, neoplasm
(phosphorylated, hypoacetylated mutant p53 raised cisplatin-induced apoptosis by activating caspase-9 independent of transcription activation, translation in bladder cancer cells TCCSUP-143-4, TCCSUP-247-5 but not in TCCSUP, TCCSUP-273-6)

IT 143313-51-3 210344-92-6, z-VDVAD-fmk 210344-95-9, z-DEVD-fmk 388114-99-6 436845-23-7 710307-43-0 774214-59-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylated, hypoacetylated mutant p53 raised cisplatin-induced apoptosis by activating caspase-9 independent of transcription activation, translation in bladder cancer cells TCCSUP-143-4, TCCSUP-247-5 but not in TCCSUP, TCCSUP-273-6)

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

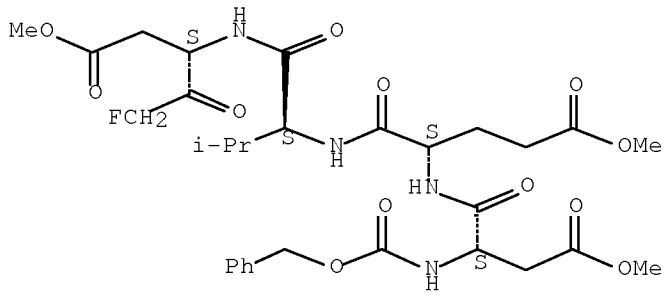
L76 ANSWER 26 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:214012 HCAPLUS Full-text
DOCUMENT NUMBER: 143:527

TITLE: Dietary bioflavonoids induce apoptosis in human leukemia cells
AUTHOR(S): Matsui, Jun; Kiyokawa, Nobutaka; Takenouchi, Hisami; Taguchi, Tomoko; Suzuki, Kyoko; Shiozawa, Yusuke; Saito, Masahiro; Tang, Wei-Ran; Katagiri, Yohko U.; Okita, Hajime; Fujimoto, Junichiro
CORPORATE SOURCE: Department of Developmental Biology, National Research Institute for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo, 154-8535, Japan
SOURCE: Leukemia Research (2005), 29(5), 573-581
CODEN: LEREDD; ISSN: 0145-2126
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dietary bioflavonoids are secondary metabolites of plants that are known to have a variety of bio-effects, including anti-cancer activity. In this study, we examined the effects of flavonoids on the growth of human leukemia cells and found that certain flavonoids induce apoptosis in a variety of human leukemia cells. The apoptosis induced by bioflavonoids was dose-dependent and was accompanied by a disruption of the mitochondrial transmembrane potential and the activation of caspase. Our data suggests that dietary bioflavonoids may be useful chemotherapeutic reagents for leukemia patients.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dietary bioflavonoids induce apoptosis in human leukemia cells)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
Section cross-reference(s): 18
IT 210344-95-9 210344-98-2, Z-IETD-fmk 220644-02-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dietary bioflavonoids induce apoptosis in human leukemia cells)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 27 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1034481 HCAPLUS Full-text
DOCUMENT NUMBER: 142:232633
TITLE: Methyl selenium-induced vascular endothelial apoptosis is executed by caspases and principally mediated by

P38 MAPK pathway
AUTHOR(S): Jiang, Cheng; Kim, Ki-Hwan; Wang, Zaisen; Lu, Junxuan
CORPORATE SOURCE: The Hormel Institute, University of Minnesota, Austin, MN, 55912, USA
SOURCE: Nutrition and Cancer (2004), 49(2), 174-183
CODEN: NUCADQ; ISSN: 0163-5581
PUBLISHER: Lawrence Erlbaum Associates, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

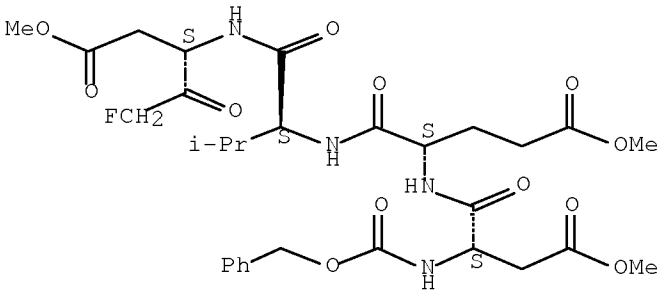
AB The induction of vascular endothelial cell apoptosis and inhibition of tumor-associated angiogenesis by selenium may contribute to its cancer chemopreventive effects. Here we, examined the stress-activated/mitogen-activated protein kinases (p38 MAPK, ERK1/2) and protein kinase B/AKT as potential signaling mediators for apoptosis induction by a methylselenol precursor methylseleninic acid (MSeA) in human umbilical vein endothelial cells (HUVEC). Time course expts. showed that p38 MAPK hyperphosphorylation and ERK1/2 dephosphorylation occurred before the cleavage of procaspase-3 and poly(ADP-ribose) polymerase (PARP), whereas AKT dephosphorylation occurred after caspase activation. The p38 MAPK inhibitor SB202190 attenuated the MSeA-induced morphol. changes and decreased DNA fragmentation and the cleavage of procaspase-3 and PARP in concordant proportions. The general caspase inhibitor zVADfmk completely blocked the MSeA-induced PARP cleavage and DNA fragmentation, whereas zDEVDfmk, an inhibitor for caspase-3-like activities, was nearly as effective for inhibiting apoptosis. In comparison, apoptosis induced by selenite in HUVECs was observed in the complete absence of an activation of the major caspases. Taken together, the data support, p38 MAPK as a key upstream mediator for the methylselenol-specific induction of vascular endothelial caspase-dependent apoptosis, which is principally executed by caspase-3-like activities.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor zDEVDfmk dose dependently blocked MSeA-induced vascular endothelial apoptotic PARP cleavage and DNA fragmentation mediated by p38MAPK pathway and executed by caspase-3 in HUVECs)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



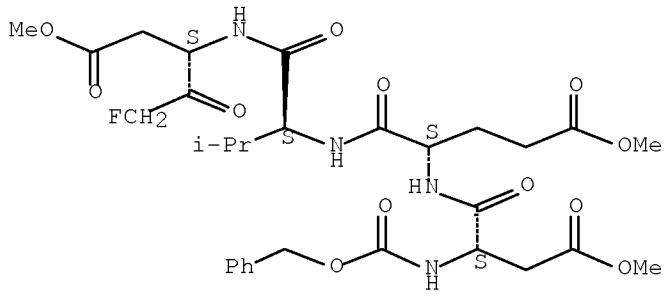
CC 1-6 (Pharmacology)

IT 169592-56-7, Caspase-3 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor zDEVDfmk dose dependently blocked MSeA-induced

vascular endothelial apoptotic PARP cleavage and DNA fragmentation mediated by p38MAPK pathway and executed by caspase-3 in HUVECs)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 28 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1005069 HCAPLUS Full-text
DOCUMENT NUMBER: 142:403550
TITLE: Caspase-dependent, geldanamycin-enhanced cleavage of co-chaperone p23 in leukemic apoptosis
AUTHOR(S): Gausdal, G.; Gjertsen, B. T.; Fladmark, K. E.; Demol, H.; Vandekerckhove, J.; Doskeland, S.-O.
CORPORATE SOURCE: Department of Biomedicine, Section of Anatomy and Cell Biology and PROBE, University of Bergen, Norway
SOURCE: Leukemia (2004), 18(12), 1989-1996
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Co-chaperone p23 is a component of the heat-shock protein (Hsp)90 multiprotein-complex and is an important modulator of Hsp90 activity. Hsp90 client proteins involved in oncogenic survival signaling are frequently mutated in leukemia, and the integrity of the Hsp90 complex could therefore be important for leukemic cell survival. We demonstrate here that p23 is cleaved to a stable 17 kDa fragment in leukemic cell lines treated with commonly used chemotherapeutic drugs. The cleavage of p23 paralleled the activation of procaspase-7 and -3 and was suppressed by the caspase-3/-7 inhibitor DEVD-FMK. In vitro translated 35S-p23 (in reticulocyte lysate) was cleaved at D142 and D145 by caspase-7 and -3. Cleavage of p23 occurred in caspase-3-deficient MCF-7 cells, suggesting a role for caspase-7 in intact cells. The Hsp90 inhibitor geldanamycin enhanced caspase-dependent p23 cleavage both in vitro and in intact cells. Geldanamycin also enhanced anthracycline-induced caspase activation and apoptosis. We conclude that p23 is a prominent target in leukemic cell apoptosis. Geldanamycin enhanced p23 cleavage both by rendering p23 more susceptible to caspases and by enhancing chemotherapy-induced caspase activation. These findings underscore the importance of the Hsp90-complex in antileukemic treatment, and suggest that p23 may have a role in survival signaling.
IT 210344-95-9, z-DEVD-fmk
RL: BSU (Biological study, unclassified); BIOL (Biological study) (caspase-3/7 inhibitor DEVD-FMK inhibited p23 indicating that caspase-3 and 7 are capable of cleaving p23 in daunorubicin treated HL-60 human leukemic cell line)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
IT Mammary gland, neoplasm
(daunorubicin and doxorubicin induced limited degradation of Hsp90 co-chaperone p23 in MCF-7 breast cancer cell line)
IT 20830-81-3, Daunorubicin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNR induced limited degradation of Hsp90 co-chaperone p23 in HL-60 human leukemic cell line, NB4 acute promyelocytic leukemia cell line, MCF-7 breast cancer cell line, GA enhanced of p23 in DNR treated HL-60 leukemic cell line)
IT 169592-56-7, Caspase-3 187389-52-2 189258-14-8, Caspase-7
192230-93-6, Pro caspase-7 201556-11-8, Pro caspase-3
210344-95-9, z-DEVD-fmk
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3/7 inhibitor DEVD-FMK inhibited p23 indicating that caspase-3 and 7 are capable of cleaving p23 in daunorubicin treated HL-60 human leukemic cell line)
IT 23214-92-8, Doxorubicin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(doxorubicin induced limited degradation of Hsp90 co-chaperone p23 in MCF-7 breast cancer cell line)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 29 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:944194 HCAPLUS Full-text
DOCUMENT NUMBER: 142:275753
TITLE: Tripeptide analogs for cancer therapy
INVENTOR(S): Liu, Keliang; Qie, Jiankun; Liang, Yuanjun; Zhao, Xiunan
PATENT ASSIGNEE(S): Institute of Toxic Medicine, Academy of Military Medical Science of PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1467220	A	20040114	CN 2002-123927	20020710
PRIORITY APPLN. INFO.:			CN 2002-123927	20020710

OTHER SOURCE(S): MARPAT 142:275753

AB The tripeptide analog, its stereoisomer, or its medical salt, A-B-C, wherein, A= L- or D-aromatic natural or nonnatural amino acid, its aromatic ring = indole, benzene, naphthalene, anthracene, phenanthrene, tetrahydroquinoline, tetrahydroisoquinoline, benzotetraisoquinoline, or their derivative substituted by halo, NO2, OH, methoxy, methylenedioxy, NH2, aminomethyl, N,N-di(C1-4 alkyl)aminomethyl, C3-7 cycloalkylaminomethyl, C3-7 heteroatom-containing cyclo-aminomethyl, sulfomethyl, or phosphonooxymethyl, and its amino may be substituted by C1-4 alkyl, C3-7 cycloalkyl, protective groups (such as benzyl, tert-butoxycarbonyl, benzyloxycarbonyl, phenoxycarbonyl, fluorenylmethoxycarbonyl, C1-5 ester group, C1-4 alkyl, or C3-7 cycloalkyl); B= natural or nonnatural lipophilic amino acid (such as Gly, Ala, Val, Leu, Ile, Pro, MeVal); and C = C1-4 alkyl-substituted gamma-amino-butyric acid, C1-4 alkyl-substituted gamma-aminobutenoic acid, substituted 3- aminobenzoic acid, (C1-4 alkyl-substituted 3- aminocyclohexenyl)formic acid, or their dipeptide. Its amino may be substituted, and benzene ring may be substituted by halo, NO2, OH, carboxy, trifluoromethyl, methylenedioxy, methylenedithio, C1-6 alkyl, C3-7 cycloalkyl, C1-5 alkoxy, NH2, or C1-5 amido, are prepared by coupling Boc-B-OH (Boc = tert-butoxycarbonyl) with C-OP (P = C1-4 alkyl) in DMF-DCM- DCC-HOBt system (DCM = dichloromethane; NMM= N-methylmorpholine; DCC = dicyclohexylcarbodiimide; HOBt = 1-hydroxybenzotriazole) to obtain Boc-B-C-OP; removing N-protective group in HCl/dioxane to obtain B-C-OP HCl; coupling with Boc-A-OH in DMF-DCM-NMM-DCC-HOBt to obtain Boc-A-B-C-OP; saponifying with LiOH/methanol-THF and acidifying with citric acid to obtain Boc-A-B-C-OH; and removing N- protective group. The tripeptide analog, its stereoisomer, or its medical salt may be used as antitumor agent.

IT 846578-42-5P

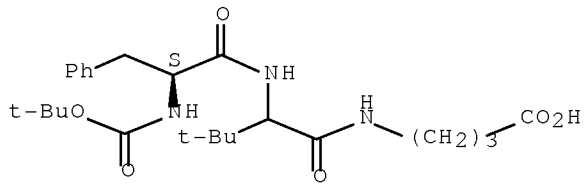
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tripeptide analogs for cancer therapy)

RN 846578-42-5 HCAPLUS

CN Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-(3-carboxypropyl)-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K007-06

ICS A61K038-08; A61P350-00

CC 6-3 (General Biochemistry)

Section cross-reference(s): 1, 13

IT Antitumor agents

Neoplasm

(tripeptide analogs for cancer therapy)

IT Tripeptides

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tripeptide analogs for cancer therapy)

IT 109-02-4

RL: RGT (Reagent); RACT (Reactant or reagent)
(treatment of; tripeptide analogs for cancer therapy)

IT 846578-00-5P 846578-30-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tripeptide analogs for cancer therapy)

IT 99-05-8 2361-96-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(tripeptide analogs for cancer therapy)

IT 939-26-4P 3251-07-8P 37439-99-9P 37447-33-9P 87360-24-5P
122745-11-3P 122745-12-4P 130887-73-9P 136015-50-4P 136015-51-5P
172214-89-0P 760912-21-8P 846578-44-7P 846578-45-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tripeptide analogs for cancer therapy)

IT 75-09-2, Dichloromethane, reactions 538-75-0, Dicyclohexylcarbodiimide 2592-95-2, 1-Hydroxybenzotriazole
RL: RGT (Reagent); RACT (Reactant or reagent)
(tripeptide analogs for cancer therapy)

IT 846578-01-6P 846578-02-7P 846578-03-8P 846578-04-9P 846578-05-0P
846578-06-1P 846578-07-2P 846578-08-3P 846578-09-4P 846578-10-7P
846578-11-8P 846578-12-9P 846578-13-0P 846578-14-1P 846578-15-2P
846578-16-3P 846578-17-4P 846578-18-5P 846578-19-6P 846578-20-9P
846578-21-0P 846578-22-1P 846578-23-2P 846578-24-3P 846578-25-4P
846578-26-5P 846578-27-6P 846578-28-7P 846578-29-8P 846578-31-2P
846578-32-3P 846578-33-4P 846578-34-5P 846578-35-6P 846578-36-7P
846578-37-8P 846578-38-9P 846578-39-0P 846578-40-3P 846578-41-4P
846578-42-5P 846578-43-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tripeptide analogs for cancer therapy)

L76 ANSWER 30 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:834434 HCAPLUS Full-text
DOCUMENT NUMBER: 142:190389
TITLE: Role of ERK Activation in Cisplatin-Induced Apoptosis in A172 Human Glioma Cells
AUTHOR(S): Choi, Byung Kwan; Choi, Chang Hwa; Oh, Hyun Lim; Kim, Yong Keun
CORPORATE SOURCE: Department of Neurosurgery, College of Medicine, Pusan National University & Medical Research Institute, Pusan, 602-739, S. Korea
SOURCE: Neurotoxicology (2004), 25(6), 915-924
CODEN: NRTXDN; ISSN: 0161-813X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cisplatin activates multiple signal transduction pathways associated with cell survival and apoptosis in various cell types. The present study was undertaken to determine the role of extracellular signal-regulated protein kinase (ERK), a member of the mitogen-activated protein kinase family, in cisplatin-induced apoptosis in human glioma cells. Cisplatin resulted in apoptosis in a dose- and time-dependent manner. Cisplatin-induced apoptosis was prevented by the hydrogen peroxide scavenger pyruvate and the antioxidant N-acetylcysteine, but not by the superoxide scavenger tiron. Western blot anal. demonstrated that cisplatin treatment induced time-dependent activation of ERK, which was inhibited by chemical inhibitors of the MEK signaling pathway (PD98059 and U0126) and N-acetylcysteine. These inhibitors prevented cisplatin-induced cell death. Transient transfection of constitutive active

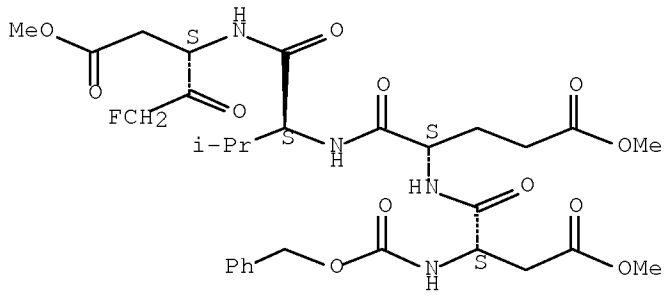
MEK1 increased cisplatin-induced apoptosis. Cisplatin resulted in a reduction in mitochondrial membrane potential and its effect was prevented by N-acetylcysteine and PD98059. Caspase inhibitors (Boc-D-FMK and zDEVD-FMK) protected against cisplatin-induced cell death. Cisplatin-induced activation of caspase-3 was inhibited by N-acetylcysteine and PD98059. Taken together, these findings suggest that the ERK activation plays an active role in mediating cisplatin-induced apoptosis of human glioma cells and functions upstream of mitochondrial dysfunction and caspase activation to the initiate the apoptotic signal.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase inhibitor Boc-D-FMK, caspase-3 inhibitor zDEVD-FMK prevented cisplatin-induced cell death and was inhibited by NAC, PD98059 indicating ERK activation act upstream of caspase activation in cisplatin-induced apoptosis in A172 cells)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

IT Human
Neuroglia, neoplasm
Signal transduction, biological
(cisplatin-induced apoptosis is mediated by activation of extracellular signal-regulated protein kinase signaling pathway and functions upstream of mitochondrial signaling including activation of caspase-3 in A172 human glioma cells)

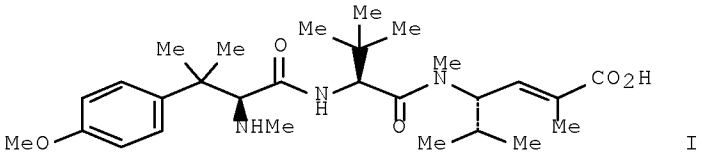
IT 169592-56-7, Caspase-3 186322-81-6, Caspase 187389-53-3, Boc-D-FMK 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase inhibitor Boc-D-FMK, caspase-3 inhibitor zDEVD-FMK prevented cisplatin-induced cell death and was inhibited by NAC, PD98059 indicating ERK activation act upstream of caspase activation in cisplatin-induced apoptosis in A172 cells)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 31 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:617803 HCAPLUS Full-text
DOCUMENT NUMBER: 141:314607
TITLE: Synthesis and Biological Activity of Analogues of the Antimicrotubule Agent

	N,β,β-Trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide (HTI-286)
AUTHOR(S):	Zask, Arie; Birnberg, Gary; Cheung, Katherine; Kaplan, Joshua; Niu, Chuan; Norton, Emily; Suayan, Ronald; Yamashita, Ayako; Cole, Derek; Tang, Zhilian; Krishnamurthy, Girija; Williamson, Robert; Khafizova, Gulnaz; Musto, Sylvia; Hernandez, Richard; Annable, Tami; Yang, Xiaoran; Discafani, Carolyn; Beyer, Carl; Greenberger, Lee M.; Loganzo, Frank; Ayral-Kaloustian, Semiramis
CORPORATE SOURCE:	Chemical and Screening Sciences, and Oncology Research, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE:	Journal of Medicinal Chemistry (2004), 47(19), 4774-4786 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 141:314607

GI



I

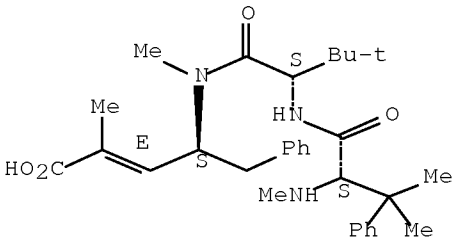
AB Hemiasterlin, a tripeptide isolated from marine sponges, induces microtubule depolymn. and mitotic arrest in cells. HTI-286, an analog from an initial study of the hemiasterlins, is presently in clin. trials. In addition to its potent antitumor effects, HTI-286 has the advantage of circumventing the P-glycoprotein-mediated resistance that hampers the efficacy of other antimicrotubule agents such as paclitaxel and vincristine in animal models. This paper describes an in-depth study of the structure-activity relationships (SAR) of analogs of HTI-286, their effects on microtubule polymerization, and their in vitro and in vivo anticancer activity. Regions of the mol. necessary for potent activity are identified. Groups tolerant of modification, leading to novel analogs, are reported. Potent analogs identified through in vivo studies in tumor xenograft models include one superior analog, HTI-042 (I).

IT 676635-58-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of analogs of peptide HTI-286 and SAR study of their anticancer activity and effects on microtubule polymerization)

RN 676635-58-8 HCAPLUS

CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(phenylmethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT Antitumor agents
Human
Neoplasm
(preparation of analogs of peptide HTI-286 and SAR study of their anticancer
activity and effects on microtubule polymerization)
IT 228266-43-1P 228266-45-3P 228266-48-6P 676633-19-5P 676633-61-7P
676633-65-1P 676633-77-5P 676633-80-0P 676633-90-2P 676634-21-2P
676634-47-2P 676634-59-6P 676634-66-5P 676634-77-8P 676634-83-6P
676634-90-5P 676634-93-8P 676635-36-2P 676635-39-5P
676635-58-8P 676636-07-0P 676636-11-6P 676636-15-0P
676636-19-4P 676636-28-5P 676636-79-6P 765930-77-6P 765930-82-3P
765930-86-7P 765930-88-9P 765931-06-4P 765931-11-1P 765931-16-6P
765931-18-8P 765931-22-4P 765931-24-6P 765931-27-9P 765931-29-1P
765931-33-7P 765931-35-9P 765931-39-3P 765931-44-0P 765931-47-3P
765931-49-5P 765931-52-0P 765931-54-2P 765931-56-4P 765931-58-6P
765931-60-0P 765931-62-2P 765931-64-4P 765931-67-7P 765931-71-3P
765931-73-5P 765931-89-3P 765931-91-7P 765931-94-0P 765931-97-3P
765932-00-1P 765932-03-4P 765932-05-6P 765932-08-9P 765932-10-3P
765932-35-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of analogs of peptide HTI-286 and SAR study of their anticancer
activity and effects on microtubule polymerization)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 32 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:446538 HCAPLUS Full-text
DOCUMENT NUMBER: 142:321
TITLE: Shikonin regulates HeLa cell death via caspase-3 activation and blockage of DNA synthesis
AUTHOR(S): Wu, Zhen; Wu, Li-Jun; Li, Lin-Hao; Tashiro, Shin-Ichi; Onodera, Satoshi; Ikejima, Takashi
CORPORATE SOURCE: Department of Pharmaceutical Science, Heilongjiang University, Harbin, 150080, Peop. Rep. China
SOURCE: Journal of Asian Natural Products Research (2004), 6(3), 155-166
CODEN: JANRFI; ISSN: 1028-6020
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Shikonin, isolated from the plant Lithospermum erythrorhizon Sieb. Et Zucc, inhibited tumor cell growth and induced cell death in various tumor cells,

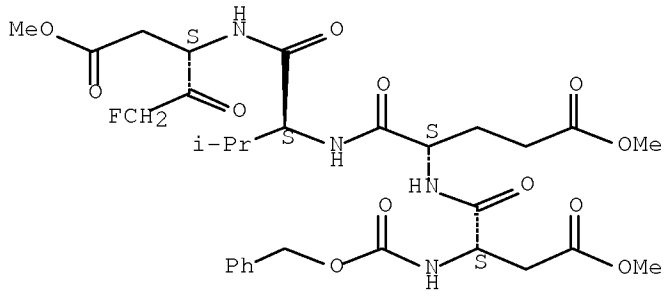
with 50% growth inhibition of human cervical cancer cells, HeLa, at 18.9±1.1 μmol L-1. Treated with 40 μmol L-1 shikonin, HeLa cells underwent marked apoptotic morphol. changes such as a round shape, membrane blebbing and apoptotic bodies derived from the fragmented nuclei. Another hallmark of apoptosis, DNA fragmentation, was observed by gel electrophoresis. Shikonin (10 μmol L-1) significantly blocked the transition from G1 to S phase in the HeLa cell cycle. Pan-caspase inhibitor (Z-VAD-FMK), caspase-3 inhibitor (Z-DEVD-FMK) or caspase-8 inhibitor (Z-IETD-FMK) effectively inhibited shikonin-induced cell death, while caspase-1 inhibitor (Ac-YVAD-CMK) and caspase-9 inhibitor (Z-LEHD-FMK) failed to affect cell death. Caspase-3 activity significantly increased within 12 h after shikonin treatment. Reduced expression of inhibitor of caspase-activated DNase (ICAD) after exposure to shikonin for 12 h suggests the resultant activation of caspase-activated DNase (CAD), leading to apoptosis.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor Z-DEVD-FMK significantly reversed shikonin-induced cell death by inhibiting reduction of ICAD expression and increase in CAD activation and blockage of transition from G1 to S phase of cell cycle in human HeLa cells)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

ST shikonin cervical cancer antitumor apoptosis DNA fragmentation caspase

IT Uterus, neoplasm
(cervix; shikonin caused cell death through caspase-3 activation by reduction of ICAD expression and increase in CAD activation and by blockage of DNA synthesis via blocking transition from G1 to S phase of cell cycle in human HeLa cells)

IT Cell proliferation
(inhibition; shikonin dose dependently inhibited cell growth in human cervical cancer HeLa cells, malignant melanoma A375-S2 cells, mouse fibrosarcoma L929 cells and MCF-7 cells)

IT Necrosis
(shikonin time dependently caused necrotic cell death in human cervical epithelial cancer HeLa cells)

IT 122191-40-6, Caspase-1 178603-78-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-1 inhibitor Ac-YVAD-CMK failed to affect shikonin-induced cell

death in human cervical epithelial cancer HeLa cells)
IT 169592-56-7, Caspase-3 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor Z-DEVD-FMK significantly reversed shikonin-induced cell death by inhibiting reduction of ICAD expression and increase in CAD activation and blockage of transition from G1 to S phase of cell cycle in human HeLa cells)
IT 180189-96-2, Caspase-9 325786-54-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-9 inhibitor Z-LEHD-FMK failed to affect shikonin-induced cell death in human cervical epithelial cancer HeLa cells)
IT 220644-02-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pan-caspase inhibitor Z-VAD-FMK effectively inhibited shikonin-induced cell death indicating that caspase family proteinase play role in human cervical epithelial cancer HeLa cell apoptosis)
IT 208939-71-3, Caspase activated deoxyribonuclease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reduction of ICAD expression and increasing caspase activated DNase activation caused apoptosis in human cervical cancer HeLa cells reversed by caspase-3 inhibitor Z-DEVD-FMK)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 33 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:267231 HCAPLUS Full-text
DOCUMENT NUMBER: 140:304081
TITLE: Preparation of peptides for treating resistant tumors
INVENTOR(S): Greenberger, Lee Martin; Loganzo, Frank, Jr.; Discafani-Marro, Carolyn Mary; Zask, Arie; Ayral-Kaloustian, Semiramis
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: PCT Int. Appl., 442 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026293	A2	20040401	WO 2003-US29832	20030918
WO 2004026293	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2406504	A1	20040320	CA 2002-2406504	20021003
AU 2003275126	A1	20040408	AU 2003-275126	20030918
US 20040121965	A1	20040624	US 2003-666722	20030918

PRIORITY APPLN. INFO.: US 2002-411883P P 20020920
WO 2003-US29832 W 20030918
OTHER SOURCE(S): MARPAT 140:304081

AB The invention provides peptides R1R2NCH(CR3R4R5)CONR6CHR7CONR8R9 [R1-R8 are H or an (un)saturated moiety having a linear, branched, or cyclic skeleton containing 1-10 (un)substituted carbon atoms and 0-4 each nitrogen, oxygen, or sulfur atoms; or R1R2N or R3R4C is a 3- to 7-membered ring; R9 is -Y-CO-Z, where Y is alkyl and Z is OH, SH, NH2, an amino acid residue, etc. (with provisos)] for treating or inhibiting the growth or eradication of tumors which are resistant to at least one chemotherapeutic agent. Thus, N,β,β-trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and shown to be a potent inhibitor of cell growth in 34 tumor cell lines (mean IC50 = 2.1 ± 1.7 nM, median 1.7 nM, range 0.2-7.3 nM) and is distinct from paclitaxel which has an usually large range of activity. The activity is independent of tumor origin and in many cases this peptide is considerably more potent than paclitaxel.

IT 676635-21-5P 676635-58-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating resistant tumors)

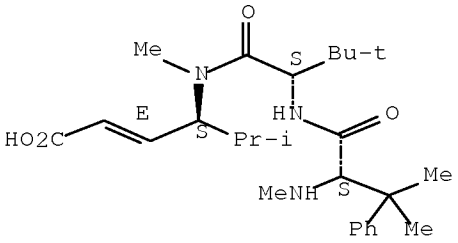
RN 676635-21-5 HCAPLUS

CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-propenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

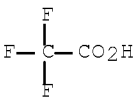
CRN 676635-20-4
CMF C26 H41 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

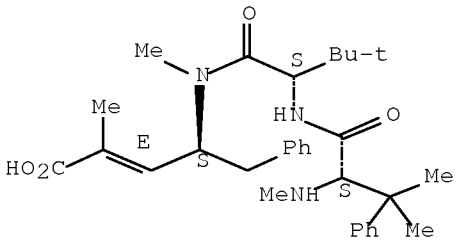
CRN 76-05-1
CMF C2 H F3 O2



RN 676635-58-8 HCAPLUS

CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(phenylmethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM A61K031-191
ICS A61K031-194; A61P035-00; A61K031-192; A61K031-195
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptide prepn antitumor resistant tumor; structure activity antitumor peptide prepn
IT P-glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MDR1; preparation of peptides for treating resistant tumors)
IT Structure-activity relationship
(antitumor; preparation of peptides for treating resistant tumors)
IT Antitumor agents
Neoplasm
(preparation of peptides for treating resistant tumors)
IT 167158-86-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MDR-1 inhibitor; preparation of peptides for treating resistant tumors)
IT 57-22-7, Vincristine 865-21-4, Vinblastine 33069-62-4, Paclitaxel 71486-22-1, Vinorelbine 114977-28-5, Docetaxel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemotherapeutic agent; preparation of peptides for treating resistant tumors)
IT 676628-40-3P 676631-63-3P 676631-71-3P 676631-78-0P 676631-86-0P
676631-94-0P 676632-03-4P 676632-11-4P 676632-20-5P 676632-31-8P
676632-40-9P 676632-45-4P 676632-48-7P 676632-66-9P 676632-69-2P
676634-25-6P 676635-06-6P 676642-03-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of peptides for treating resistant tumors)
IT 169181-24-2P 228266-42-0P 228266-48-6P 228266-49-7P 500229-47-0P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating resistant tumors)

IT 676637-30-2P 676637-32-4P 676637-34-6P 676637-75-5P 676637-78-8P
676643-79-1P 676643-80-4P 676643-82-6P 676643-83-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating resistant tumors)

IT 64-04-0, Phenethylamine 75-03-6, Iodoethane 98-03-3, Thiophene-2-aldehyde 98-80-6, Phenylboronic acid 100-66-3, Methoxybenzene, reactions 104-87-0 104-88-1, p-Chlorobenzaldehyde, reactions 111-87-5, 1 Octanol, reactions 114-76-1, Phenylpyruvic acid sodium salt 151-10-0, 1,3-Dimethoxybenzene 151-18-8, 3 Aminopropionitrile 156-06-9 328-51-8, 2-Oxooctanoic acid 456-48-4, m-Fluorobenzaldehyde 461-72-3, Hydantoin 498-62-4, Thiophene-3-aldehyde 529-20-4, o-Tolualdehyde 540-51-2, 2 Bromoethanol 543-24-8, Acetylglycine 556-82-1, 3 Methyl 2 buten 1 ol 587-04-2, m-Chlorobenzaldehyde 591-31-1, m-Anisaldehyde 620-23-5, m-Tolualdehyde 628-21-7, 1,4-Diiodobutane 628-77-3, 1,5-Diiodopentane 636-72-6, 2 Thiophenemethanol 710-11-2, 2-Oxo-4-phenylbutyric acid 759-05-7

939-97-9, p tert-Butylbenzaldehyde 1121-57-9, 1 Isocyanocyclohexene
2280-27-5 2605-67-6 3132-99-8, m-Bromobenzaldehyde 3282-30-2,
Pivaloyl chloride 3541-37-5, Thianaphthene-2-carboxaldehyde 4530-20-5
5381-20-4, Thianaphthene-3-carboxaldehyde 5717-37-3,
(Carbethoxyethylidene)triphenylphosphorane 5779-95-3,
3,5-Dimethylbenzaldehyde 5973-71-7, 3,4-Dimethylbenzaldehyde
13139-15-6 13734-34-4, N-tert-Butoxycarbonyl-L-phenylalanine
18962-05-5, 4-Isopropoxybenzaldehyde 21744-88-7,
Cyclopropanecarboxaldehyde, 1 phenyl 23082-30-6 25080-84-6
40447-58-3 55447-00-2 59752-74-8 64263-80-5 90600-20-7
91159-79-4 97674-02-7, Tributyl(1-ethoxyvinyl)tin 100564-78-1
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptides for treating resistant tumors)

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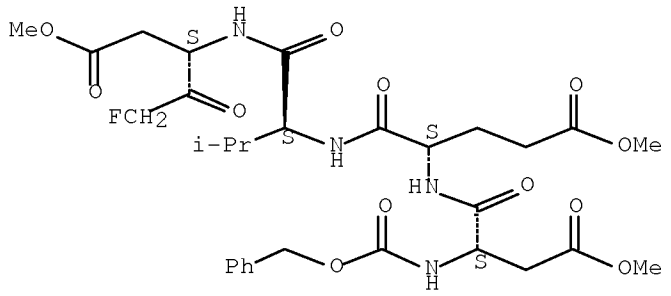
676630-91-4P 676631-04-2P 676631-23-5P 676631-26-8P 676636-30-9P
676636-32-1P 676636-34-3P 676636-35-4P 676636-38-7P 676636-40-1P

676636-42-3P 676636-45-6P 676636-47-8P 676636-49-0P 676636-51-4P
676636-59-2P 676637-05-1P 676637-07-3P 676637-13-1P 676637-15-3P
676637-17-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for treating resistant tumors)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 34 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:165793 HCAPLUS Full-text
DOCUMENT NUMBER: 141:199623
TITLE: Five-lipoxygenase-activating protein inhibitor MK-886 induces apoptosis in gastric cancer through upregulation of p27kip1 and bax
AUTHOR(S): Fan, Xiao Ming; Tu, Shui Ping; Lam, Shiu Kum; Wang, Wei Ping; Wu, Jing; Wong, Wai Man; Yuen, Man Fung; Lin, Marie Chia Mi; Kung, Hsiang Fu; Wong, Benjamin Chun-Yu
CORPORATE SOURCE: Department of Medicine, Fudan University Affiliated Jinshan Hospital, Shanghai, Peop. Rep. China
SOURCE: Journal of Gastroenterology and Hepatology (2004), 19(1), 31-37
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and Aim: Products of the arachidonic acid metabolizing enzyme, 5-lipoxygenase (5-LOX), stimulate the growth of several cancer types. Inhibitors of 5-LOX and 5-LOX-activating protein (FLAP) induce apoptosis in some cancer cells. Here, the authors investigated the effect of a FLAP inhibitor, MK-886, on the inhibition of proliferation and induction of apoptosis in gastric cancer. Methods: Cell proliferation in gastric cancer cells was measured using an 3-(4,5-dimethyl-2 thiazoyl)-2,5-diphenyl-2H-tetrazolium bromide assay. Apoptosis was measured using acridine orange staining and flow cytometry. Protein expression of apoptosis-related genes p53, p21waf1, p27kip1, bcl-2 families, cytochrome c, and the caspases were examined using Western blotting. Caspase-3 activity was measured using colorimetric assay of substrate cleavage. Results: MK-886 inhibited cell growth in a dose- and time-dependent manner. Apoptosis was induced in gastric cancer cells and was characterized by upregulation of p27kip1 and bax, with release of cytochrome c from mitochondria into cytosol, which initiated caspase-3 activation. Specific caspase-3 inhibitors partially blocked MK-886-induced apoptosis. Conclusion: The present results suggest that MK-886 induces apoptosis in gastric cancer cells through upregulation of p27kip1 and bax, and that MK-886 is a potentially useful drug in gastric cancer prevention and therapy.
IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
ST lipoxygenase activating protein inhibitor apoptosis gastric cancer ; bax caspase
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; FLAP inhibitor MK-886 upregulated bax protein in gastric cancer cell AGS)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FLAP (arachidonate lipoxygenase-activating protein); FLAP inhibitor MK-886 induced apoptosis through upregulation of p27kip1 and bax, in gastric cancer cells)
IT Drug targets
(FLAP inhibitor MK-886 induced apoptosis through upregulation of p27kip1 and bax while caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cells)
IT Apoptosis
(FLAP inhibitor MK-886 induced apoptosis through upregulation of p27kip1 and bax, release of cytochrome c and activation of caspase-3 in gastric cancer cells)
IT Human
(FLAP inhibitor MK-886 inhibited cell growth dose and time-dependently, induced apoptosis through upregulation of p27kip1 and bax, release of cytochrome c and activation of caspase-3 in gastric cancer cell AGS)
IT Cell cycle
(MK-886 caused cell increase in G0/G1 phase and slight cell decrease in G2 and S phase in gastric cancer cells)
IT Stomach, neoplasm
(caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
IT p53 (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
IT Cell proliferation
(inhibition; caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p21CIP1; caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced

apoptosis in gastric cancer cell AGS)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p27KIP1; caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
IT 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FLAP inhibitor MK-886 induced apoptosis through upregulation of p27kip1 and bax, in gastric cancer cells)
IT 118414-82-7, MK-886
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLAP inhibitor MK-886 induced apoptosis through upregulation of p27kip1 and bax, release of cytochrome c and activation of caspase-3 in gastric cancer cells)
IT 9007-43-6, Cytochrome c, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MK-886 induced cytochrome C release from mitochondria to cytosol in gastric cancer cell AGS)
IT 169592-56-7, Caspase-3 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caspase-3 inhibitor, z-DEVD-fmk blocked MK-886 induced apoptosis in gastric cancer cell AGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 35 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:912578 HCAPLUS Full-text
DOCUMENT NUMBER: 140:5305
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and a tachykinin receptor antagonist
INVENTOR(S): Yao, Sui-Long; Jones, Raymond E.; Defeo-Jones, Deborah; Heimbrook, David C.; Rhymer, Patricia; Wasserbly, Pamela J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 107 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030215456	A1	20031120	US 2001-969322	20011002

PRIORITY APPLN. INFO.: US 2001-969322 20011002
OTHER SOURCE(S): MARPAT 140:5305
AB The invention relates to methods of treating cancer using a combination of a compound which is a PSA conjugate and a tachykinin receptor antagonist and to methods of preparing such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) (synthesis given) and an example of a tachykinin receptor antagonist is 4-(1,2,4-triazol-3-ylmethyl)-2(S)-[3,5-bis(trifluoromethyl)benzyloxy]-3(S)- phenylmorpholine.
IT 301296-26-4P 301296-27-5P 301296-52-6P
301296-53-7P 301296-54-8P 627082-03-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

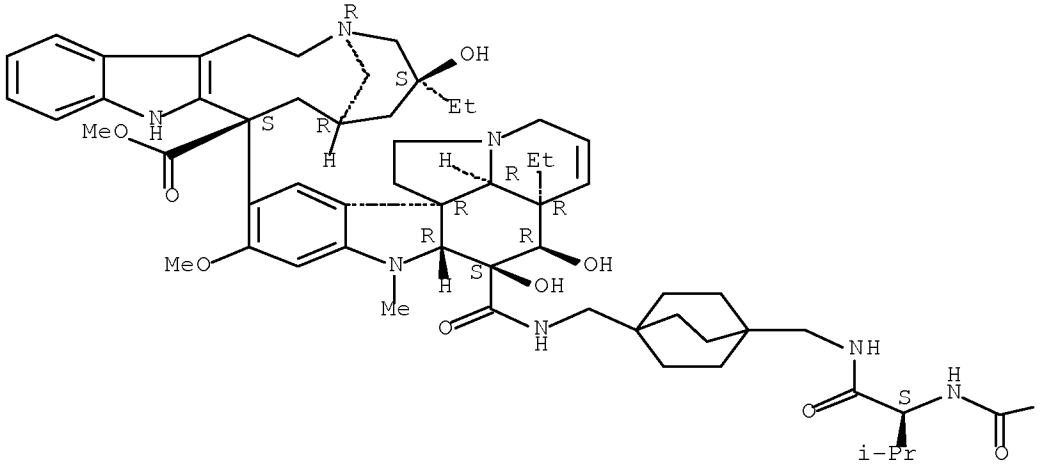
(Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)

RN 301296-26-4 HCAPLUS

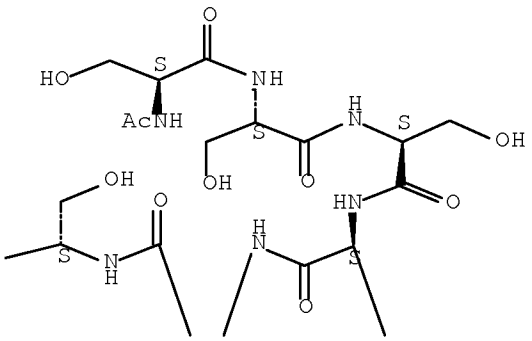
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

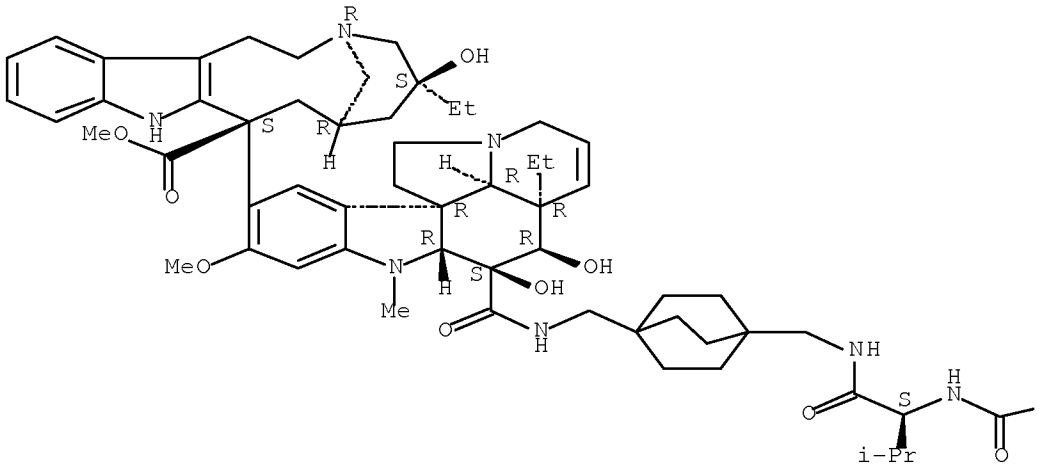
RN 301296-27-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 301296-26-4
CMF C85 H124 N14 O20

Absolute stereochemistry.

PAGE 1-A



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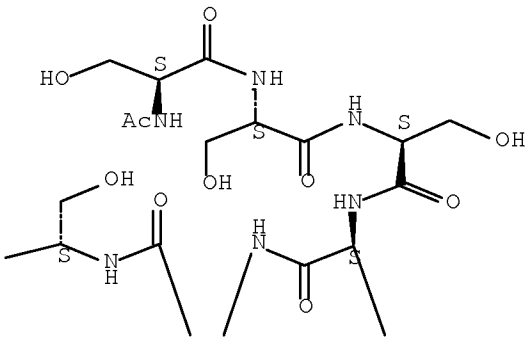
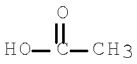


PAGE 2-B

CM 2

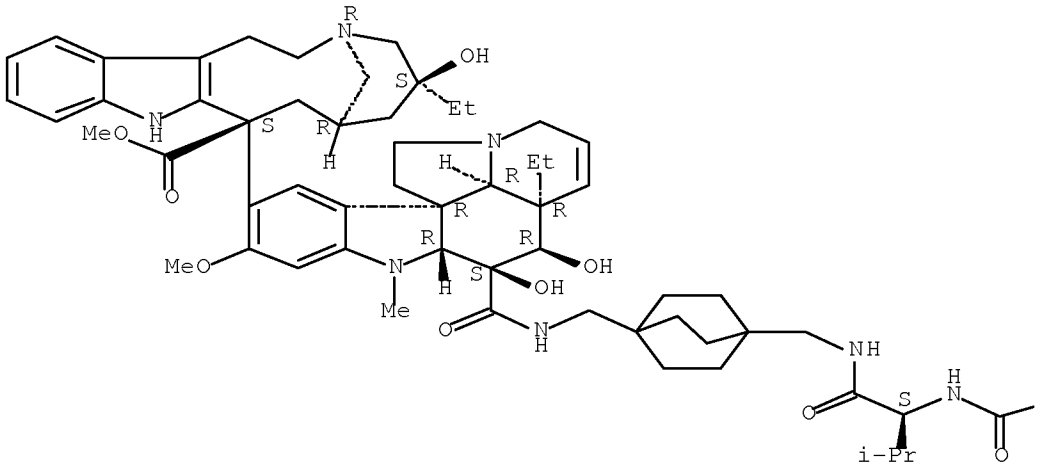
CRN 64-19-7
CMF C2 H4 O2



RN 301296-52-6 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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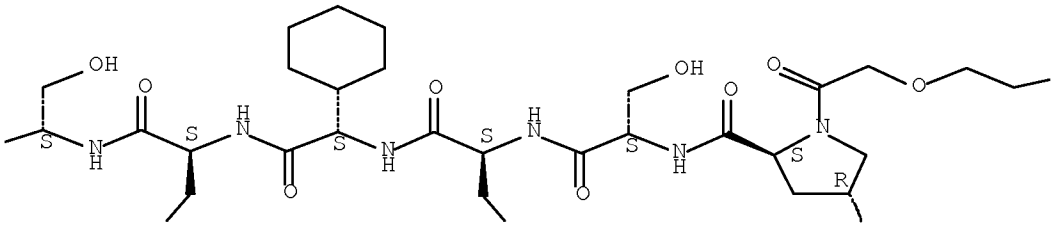
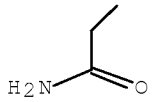


PAGE 1-C

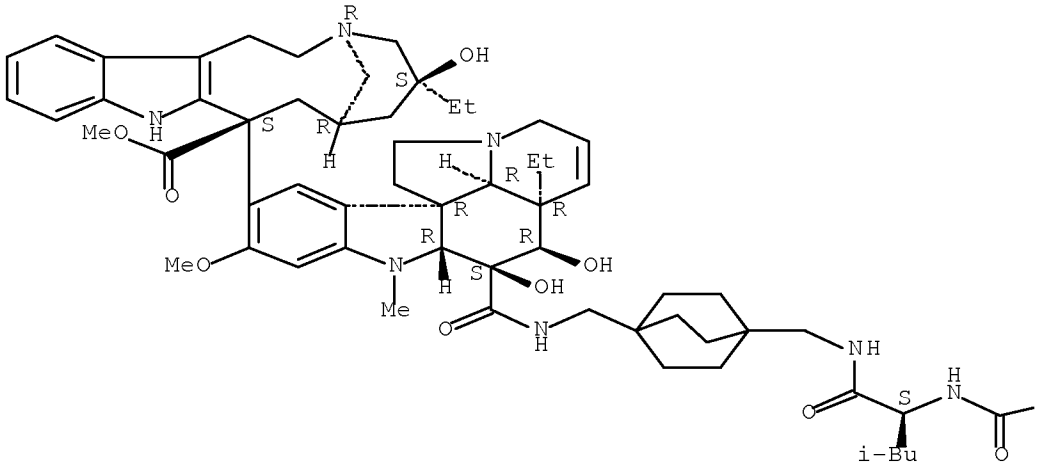
PAGE 2-B



RN 301296-53-7 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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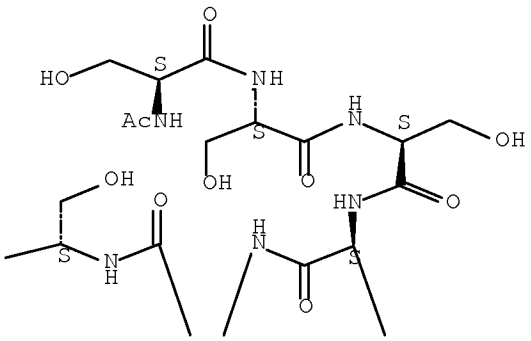
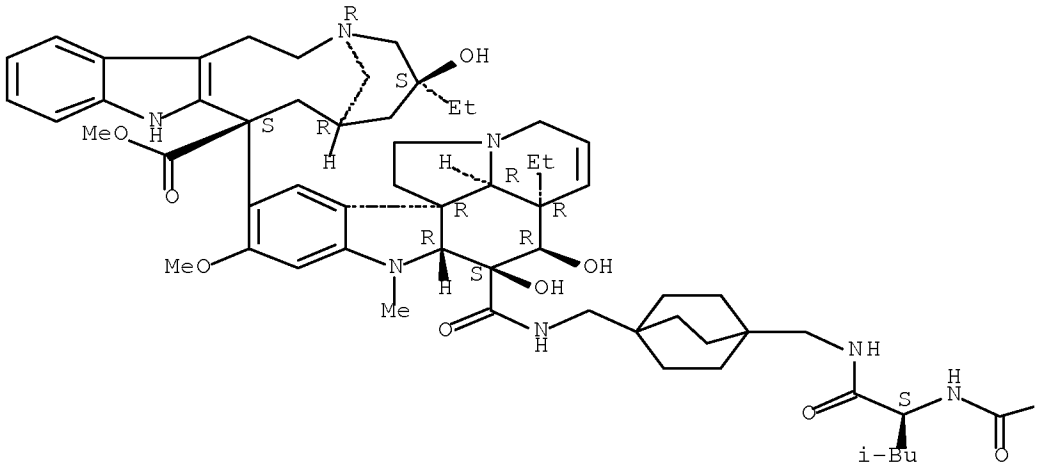


PAGE 2-B

RN 301296-54-8 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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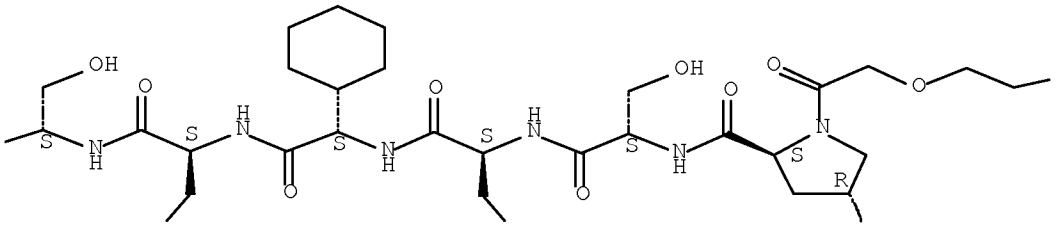
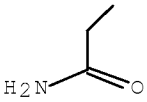


PAGE 1-C

PAGE 2-B



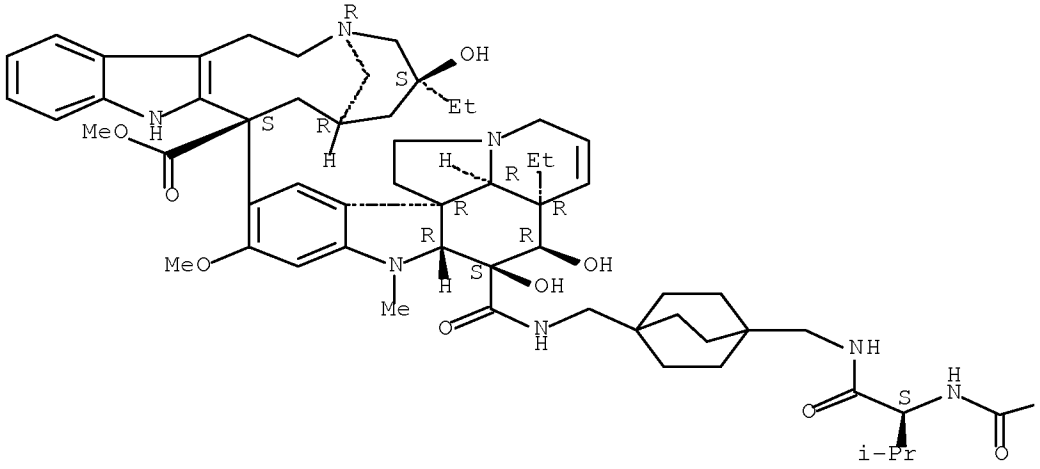
RN 627082-03-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

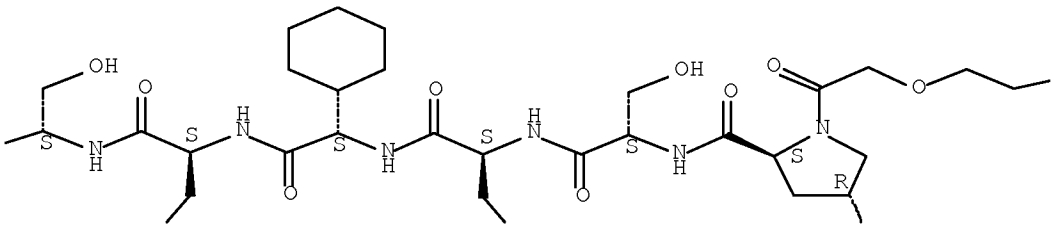
CRN 301296-52-6
CMF C92 H136 N14 O23

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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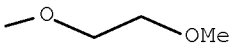

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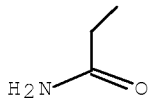
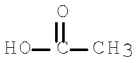


CM 2

CRN 64-19-7
CMF C2 H4 O2



IC ICM A61K039-00
ICS A61K038-14
INCL 424185100; 424277100; 514008000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT Drug delivery systems
(prodrugs; treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT Antitumor agents
Neoplasm
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT Amino acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT 174639-73-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT 627082-00-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)
IT 136982-36-0P 138449-07-7P 145742-28-5P 153438-49-4P 155418-05-6P
158647-50-8P 159706-38-4P 159706-39-5P 159706-67-9P 159706-90-8P
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627082-83-1P 627082-99-9P 627083-01-6P 627083-03-8P 627083-05-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)

IT 104-63-2, n Benzylethanolamine 143-67-9, Vinblastine sulfate 298-12-4, Glyoxylic acid 352-13-6, 4 Fluorophenylmagnesium bromide 402-31-3, 1 3 Bis trifluoromethyl benzene 24238-86-6 37577-28-9, 1s 2r + Norephedrine 155742-64-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)

IT 328-70-1P 3352-69-0P 30071-93-3P 55383-37-4P 117037-25-9P
127852-28-2P 171482-05-6P 200000-59-5P 205186-83-0DP, resin-bound
205186-83-0P 207395-79-7P 207395-87-7DP, resin-bound 207395-89-9DP, resin-bound 207395-89-9P 207395-91-3DP, resin-bound 207395-92-4P
219996-49-3P 219996-50-6P 219996-51-7P 219996-52-8P 226969-87-5P
243127-40-4P 243127-46-0P 243127-56-2P 243127-57-3P 287930-73-8P
287930-75-0P 301296-38-8P 301296-39-9P 301296-40-2P 301296-41-3P
301296-42-4P 301296-49-1DP, resin-bound 301296-49-1P 301296-50-4P
318255-60-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)

IT 77-48-5, 1 3 Dibromo 5 5 dimethylhydantoin
RL: RGT (Reagent); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and tachykinin receptor antagonist)

IT 174639-48-6 174639-56-6 174639-60-2 174639-87-3 174640-46-1
174640-54-1 174640-55-2 174640-56-3 174640-57-4 174640-77-8
189508-82-5 305326-07-2 476370-93-1 476370-94-2 476370-95-3
476370-96-4 627580-69-2 627580-70-5 627580-71-6 627580-72-7
627580-73-8 627580-74-9 627580-75-0 627580-76-1 627580-77-2
627580-78-3 627580-79-4 627580-80-7 627580-81-8
RL: PRP (Properties)
(unclaimed protein sequence; treatment of cancer with a prostate specific antigen (PSA) conjugate and a tachykinin receptor antagonist)

L76 ANSWER 36 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:903368 HCAPLUS Full-text
DOCUMENT NUMBER: 140:385588
TITLE: Apoptosis-mediated selective killing of malignant cells by cardiac steroids: maintenance of cytotoxicity and loss of cardiac activity of chemically modified derivatives
AUTHOR(S): Daniel, Dinara; Susal, Caner; Kopp, Brigitte; Opelz, Gerhard; Terness, Peter

CORPORATE SOURCE: Institute of Immunology, Department of Transplantation Immunology, University of Heidelberg, Heidelberg, 69120, Germany
SOURCE: International Immunopharmacology (2003), 3(13-14), 1791-1801
CODEN: IINMBA; ISSN: 1567-5769
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

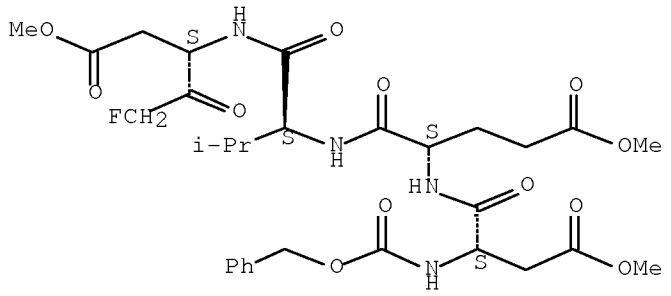
AB Cardiac glycosides are commonly used drugs in clin. medicine. We analyzed the cytotoxic effect of six steroids belonging to the bufadienolide family on malignant T lymphoblasts and normal peripheral blood mononuclear cells (PBMC). One compound was a natural bufadienolide glycoside (hellebrin) with cardiac activity. The other five compds. were chemical modified derivs. that did not contain cardioactive groups. We found that these steroids were able to cause time-dependent apoptosis in Jurkat T lymphoblasts, whereas they only minimally affected PBMC. Preferential killing of malignant cells was induced by the natural cardioactive substance hellebrin and by three of the five chemical modified non-cardioactive derivs. The substances caused mitochondrial transmembrane potential disruption and internucleosomal DNA fragmentation in tumor cells. The cytoplasmic and nuclear events of bufadienolide-induced apoptosis were strongly inhibited in the presence of caspase 8, caspase 9, or caspase 3 inhibitors, as well as in the presence of the broad-spectrum caspase inhibitor Z-VAD-FMK. Overexpression of Bcl-2 significantly protected bufadienolide-treated cells from phosphatidylserine translocation, transmembrane potential disruption, and internucleosomal DNA fragmentation. Our results show that the analyzed bufadienolide derivs. preferentially kill malignant human lymphoblasts by initiating apoptosis via the classical caspase-dependent pathway. Apoptosis-inducing agents specific for tumor cells might be ideal anti-tumor drugs. The therapeutic use of bufadienolides has been hampered by their concomitant cardiac activity. The description of compds. without cardiac activity but with tumor-specific cytotoxicity suggests the potential of using them in cancer therapy.

IT 210344-95-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis-mediated selective killing of malignant cells by cardiac steroids)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)
Section cross-reference(s): 7
ST cardiac steroid cancer apoptosis pathway caspase inhibitor ZVADFMK
IT 13289-18-4, Hellebrin 17008-79-6 23449-32-3 29565-35-3D, Bufadienolide, compds. 125496-63-1 210344-95-9 220644-02-0 220760-26-9 325786-54-7 336183-69-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis-mediated selective killing of malignant cells by cardiac steroids)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 37 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:551331 HCAPLUS Full-text
DOCUMENT NUMBER: 139:129670
TITLE: Modulation of mitochondrial remodeling by BH3 interacting domain death agonist and uses in treating apoptosis
INVENTOR(S): Korsmeyer, Stanley
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, Inc., USA; Scorrano, Luca
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057158	A2	20030717	WO 2002-US41789	20021230
WO 2003057158	A3	20040212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2471719	A1	20030717	CA 2002-2471719	20021230
AU 2002364364	A1	20030724	AU 2002-364364	20021230
US 20030224986	A1	20031204	US 2002-334006	20021230
US 7247700	B2	20070724		
EP 1469871	A2	20041027	EP 2002-799347	20021230
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20080097081	A1	20080424	US 2007-818915	20070615

PRIORITY APPLN. INFO.:

US 2001-345733P	P	20011231
US 2002-382207P	P	20020521
US 2002-334006	A3	20021230
WO 2002-US41789	W	20021230

AB This invention relates generally to methods and compns. for the regulation of apoptosis and novel BH3 interacting domain death agonist, BID, polypeptide variants of BID, and the polynucleotides encoding them for modulating mitochondrial remodeling, the release of cytochrome c store in mitochondrial

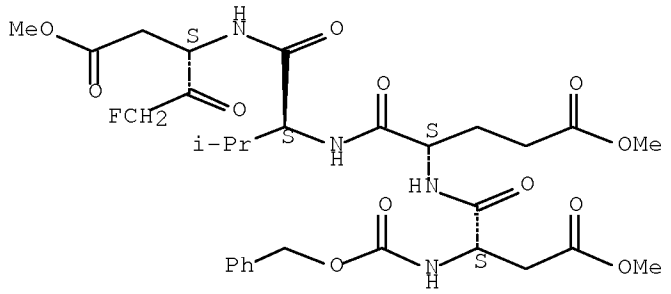
cristae and apoptosis. Also disclosed are antibodies that immunospecifically bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the novel polypeptide, polynucleotide, or antibody specific to the polypeptide. Vectors, host cells, antibodies and recombinant methods for producing the polypeptides and polynucleotides, as well as methods for using same are also included. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of apoptosis associated disorders involving these novel human nucleic acids and proteins.

IT 210344-95-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as caspase inhibitor; modulation of mitochondrial remodeling by BH3 interacting domain death agonist and uses in treating apoptosis)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K

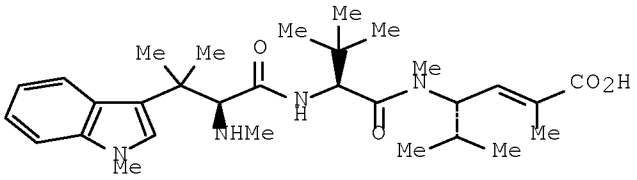
CC 6-1 (General Biochemistry)
Section cross-reference(s): 1, 3, 13

IT AIDS (disease)
Autoimmune disease
Fertility disorders
Immunodeficiency
Neoplasm
(treatment of; modulation of mitochondrial remodeling by BH3 interacting domain death agonist and uses in treating apoptosis)

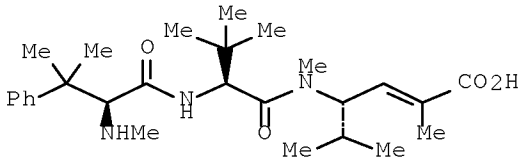
IT 9067-75-8, Transglutaminase 80146-85-6, Transglutaminase 86480-67-3, Ubiquitin C-terminal hydrolase 137741-97-0, Transglutaminase 210344-95-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as caspase inhibitor; modulation of mitochondrial remodeling by BH3 interacting domain death agonist and uses in treating apoptosis)

L76 ANSWER 38 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:58 HCAPLUS Full-text
DOCUMENT NUMBER: 138:205332
TITLE: Synthesis and Antimitotic/Cytotoxic Activity of Hemiasterlin Analogues
AUTHOR(S): Nieman, James A.; Coleman, John E.; Wallace, Debra J.;

Piers, Edward; Lim, Lynette Y.; Roberge, Michel; Andersen, Raymond J.
CORPORATE SOURCE: Department of Chemistry and Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC, V6T 1Z1, Can.
SOURCE: Journal of Natural Products (2003), 66(2), 183-199
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:205332
GI



I



II

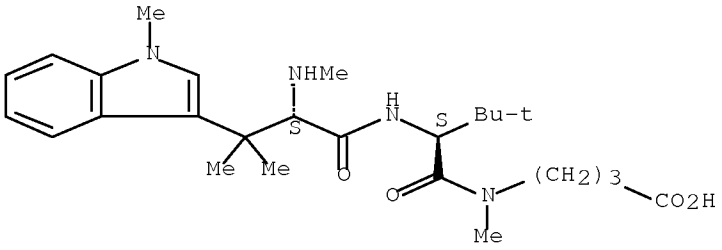
AB The antimitotic sponge tripeptide hemiasterlin (I) and several of its structural analogs have been synthesized and evaluated in cell-based assays for both cytotoxic and antimitotic activity in order to explore the SAR for this promising anticancer drug lead. One synthetic hemiasterlin analog, SPA110, II, showed more potent in vitro cytotoxicity and antimitotic activity than the natural product hemiasterlin, and consequently it has been subjected to thorough preclin. evaluation and targeted for clin. evaluation. The details of the synthesis of hemiasterlin and the analogs and a discussion of how their biol. activities vary with their structures are presented in this paper.

IT 500229-37-8P 500229-38-9P 500229-39-0P
500229-41-4P 500229-44-7P 500229-45-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antimitotic/cytotoxic activity of peptide hemiasterlin analogs as anticancer agents)

RN 500229-37-8 HCAPLUS

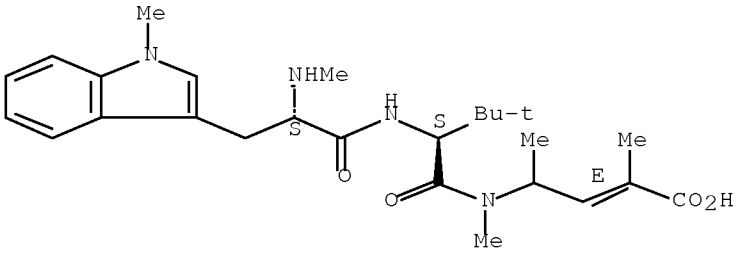
CN L-Valinamide, N,β,β,1-tetramethyl-L-tryptophyl-N-(3-carboxypropyl)-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



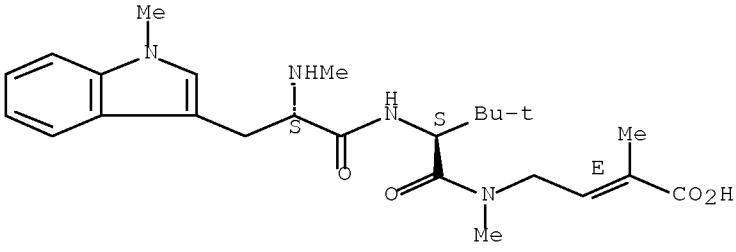
RN 500229-38-9 HCAPLUS
CN L-Valinamide, N,1-dimethyl-L-tryptophyl-N-[(2E)-3-carboxy-1-methyl-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



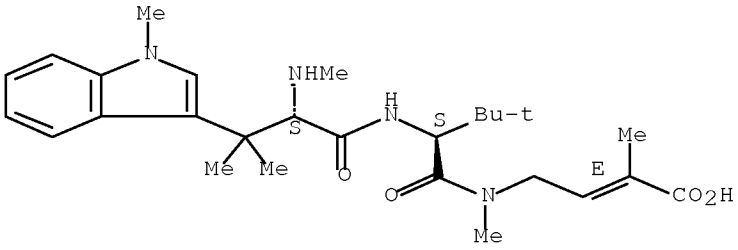
RN 500229-39-0 HCAPLUS
CN L-Valinamide, N,1-dimethyl-L-tryptophyl-N-[(2E)-3-carboxy-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 500229-41-4 HCAPLUS
CN L-Valinamide, N,β,β,1-tetramethyl-L-tryptophyl-N-[(2E)-3-carboxy-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

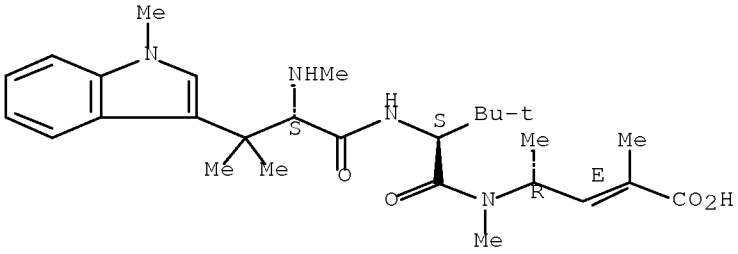
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 500229-44-7 HCAPLUS

CN L-Valinamide, N,β,β,1-tetramethyl-L-tryptophyl-N-[(1R,2E)-3-carboxy-1-methyl-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

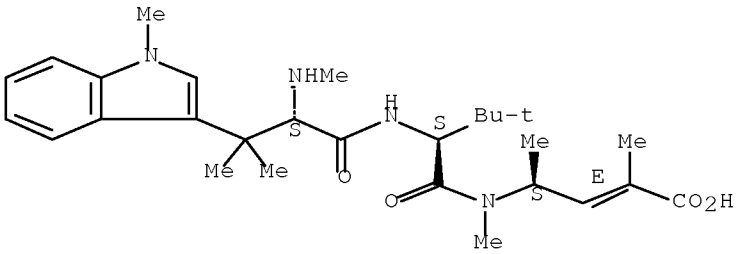
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 500229-45-8 HCAPLUS

CN L-Valinamide, N,β,β,1-tetramethyl-L-tryptophyl-N-[(1S,2E)-3-carboxy-1-methyl-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT 500229-60-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

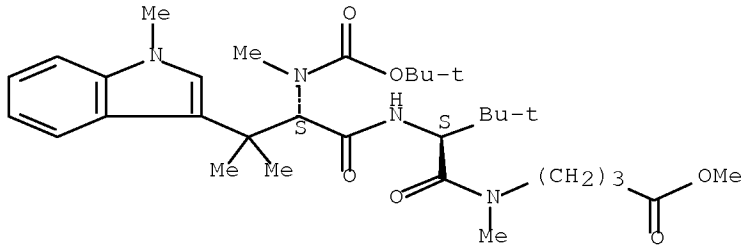
(preparation and antimitotic/cytotoxic activity of peptide hemiasterlin analogs as anticancer agents)

RN 500229-60-7 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-N,β,β,1-tetramethyl-L-tryptophyl-N-(4-methoxy-4-oxobutyl)-N,3-dimethyl- (9CI) (CA

INDEX NAME)

Absolute stereochemistry.



CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT Antitumor agents
Human
Neoplasm
(preparation and antimitotic/cytotoxic activity of peptide hemiasterlin analogs as anticancer agents)
IT 157207-90-4P, Hemiasterlin 169181-24-2P, Hemiasterlin A 169181-25-3P, Hemiasterlin B 169181-27-5P, Criamide B 179939-69-6P, Hemiasterlin methyl ester 184434-35-3P, Dihydrohemiasterlin 228266-40-8P, SPA 110 228266-42-0P 228266-44-2P 228266-46-4P 228266-48-6P 228266-50-0P 228266-52-2P 246847-61-0P 500229-30-1P 500229-31-2P 500229-33-4P 500229-34-5P 500229-35-6P 500229-36-7P 500229-37-8P 500229-38-9P 500229-39-0P 500229-40-3P 500229-41-4P 500229-42-5P 500229-43-6P 500229-44-7P 500229-45-8P 500229-46-9P 500229-47-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antimitotic/cytotoxic activity of peptide hemiasterlin analogs as anticancer agents)
IT 1010-48-6P 1912-33-0P 37553-65-4P 72228-40-1P 96021-69-1P 132631-08-4P 138802-17-2P 160711-20-6P 184434-17-1P 184434-20-6P 184434-21-7P 184434-22-8P 184434-23-9P 184434-24-0P 184434-25-1P 184434-26-2P 184434-27-3P 184434-28-4P 187345-37-5P 187345-39-7P 187345-40-0P 228266-34-0P 228266-35-1P 228266-36-2P 228266-39-5P 244033-82-7P 500229-32-3P 500229-48-1P 500229-49-2P 500229-50-5P 500229-51-6P 500229-52-7P 500229-53-8P 500229-54-9P 500229-55-0P 500229-56-1P 500229-57-2P 500229-58-3P 500229-59-4P 500229-60-7P 500229-61-8P 500229-63-0P 500229-65-2P 500229-67-4P 500229-69-6P 500229-71-0P 500229-73-2P 500229-75-4P 500229-77-6P 500229-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antimitotic/cytotoxic activity of peptide hemiasterlin analogs as anticancer agents)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 39 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:889545 HCAPLUS Full-text
DOCUMENT NUMBER: 138:301
TITLE: Method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a

cytotoxic agent in combination with radiation therapy
INVENTOR(S): Yao, Sui-long; Jones, Raymond E.; Defeo-Jones, Deborah; Heimbrook, David C.; Rhymer, Patricia; Wasserbly, Pamela J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20020173451	A1	20021121	US 2001-969244		20011002
PRIORITY APPLN. INFO.:			US 2000-242815P	P	20001024

OTHER SOURCE(S): MARPAT 138:301

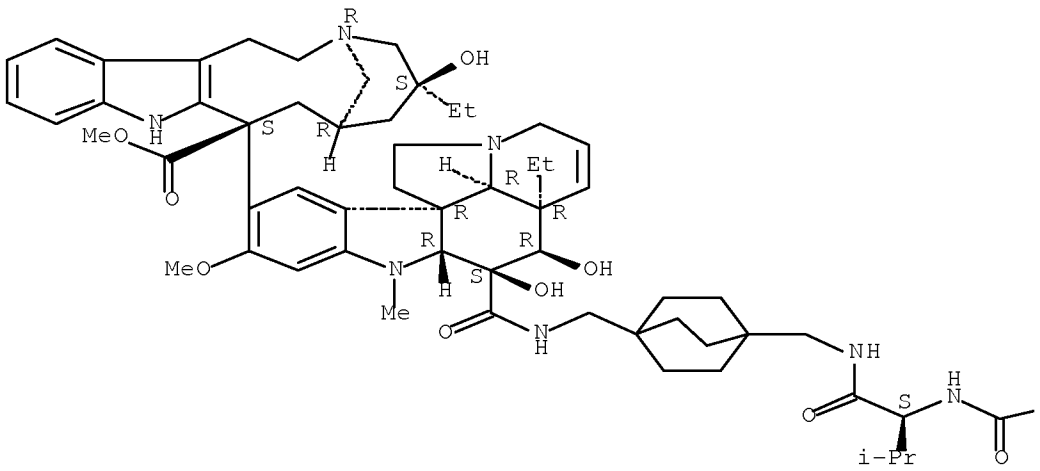
AB The present invention relates to a method of treating cancer, and more particularly cancer associated with cells that produce and secrete prostate specific antigen (PSA), which is comprised of administering to a patient in need of such treatment a therapeutically effective amount of at least one conjugate (hereinafter referred to as a PSA conjugate), which comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent, in combination with radiation therapy. The preparation of conjugates of doxorubicin and vinblastine is presented.

IT 219996-17-5P 219996-19-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

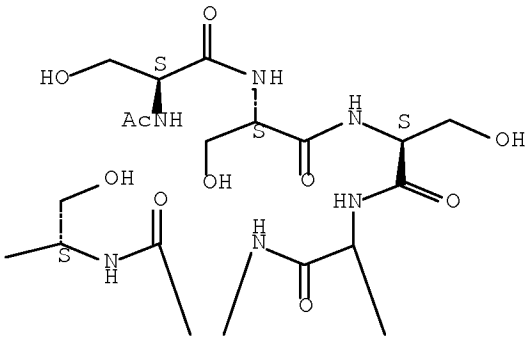
RN 219996-17-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

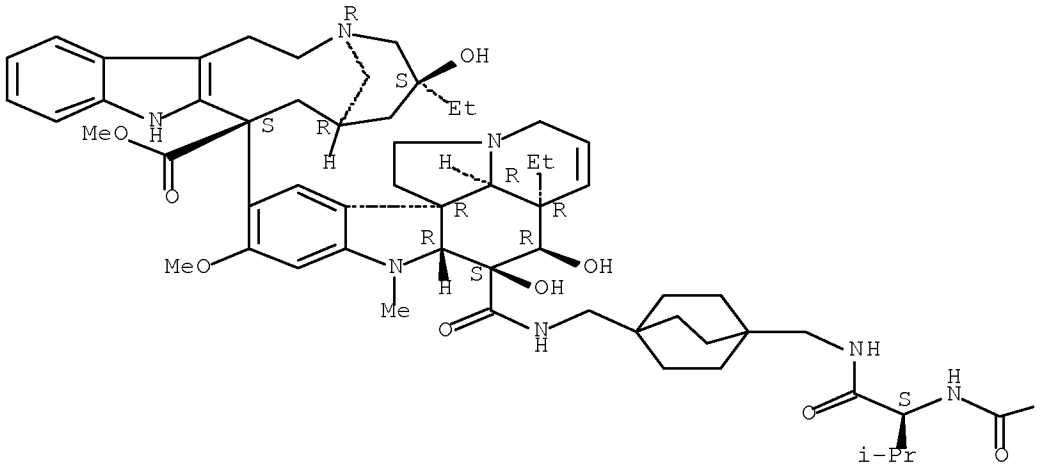


PAGE 2-B

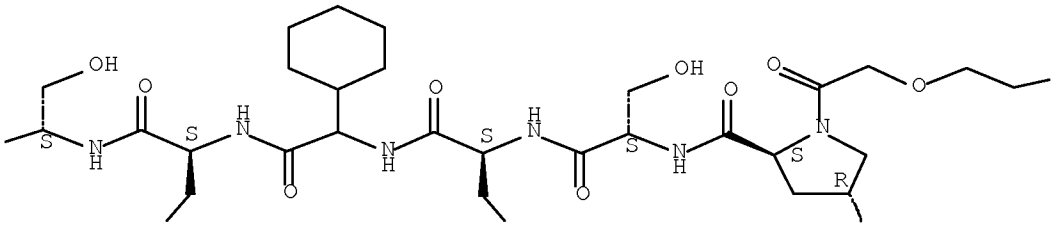
RN 219996-19-7 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

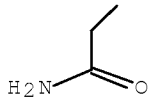


PAGE 1-B



PAGE 1-C

PAGE 2-B



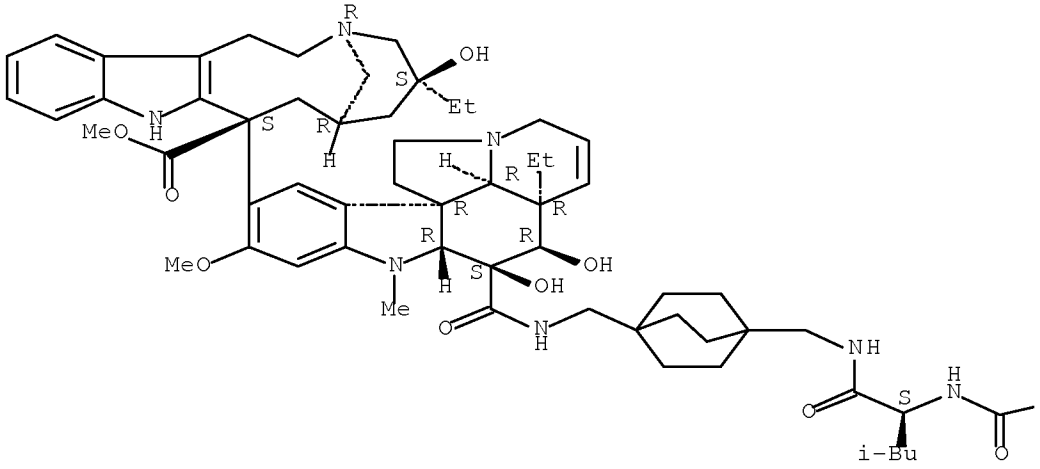
IT 219996-18-6 219996-20-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

RN 219996-18-6 HCAPLUS

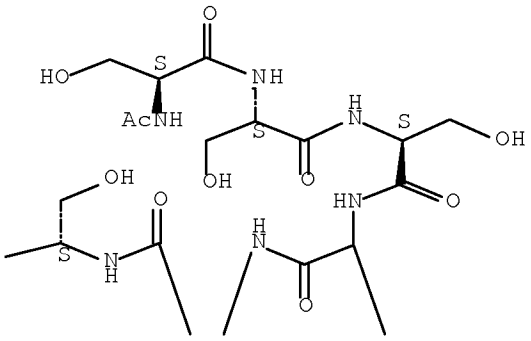
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

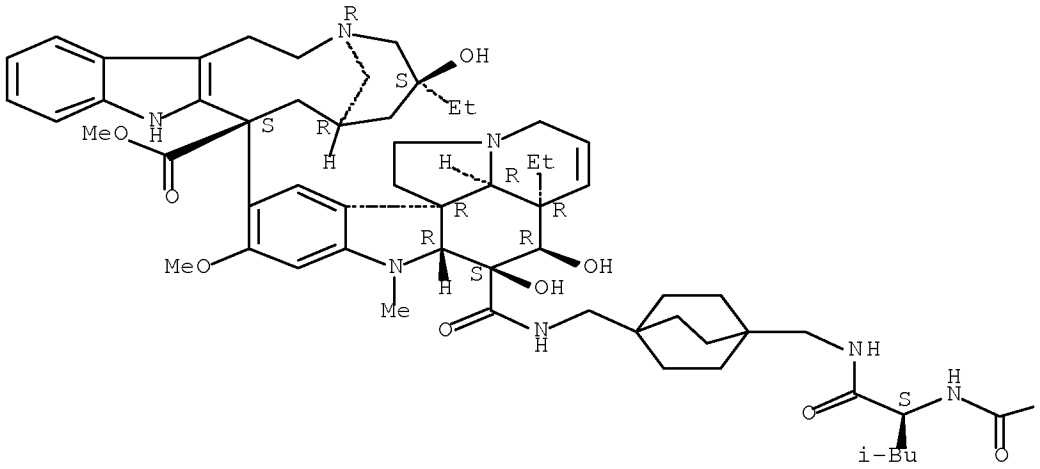


PAGE 2-B

RN 219996-20-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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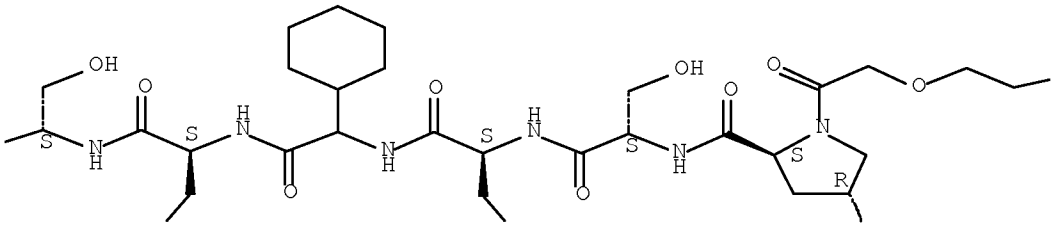
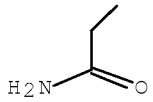


PAGE 1-C

PAGE 2-B



IC ICM A61K038-16
ICS C07K009-00; A61N005-00
INCL 514008000; 600001000; 530322000; 530395000
CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 26, 27, 34, 63
ST PSA cleavable conjugate cytotoxic agent cancer treatment
IT Prostate gland, disease
(benign hyperplasia; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)
IT Hyperplasia
(benign prostatic; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)
IT Prostate gland, neoplasm
(carcinoma; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)
IT Antitumor agents
Neoplasm
Prostate gland, neoplasm
Radiotherapy
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)
IT Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)
IT Drug delivery systems
(prodrugs; method of treating cancer using conjugate of

oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT Antitumor agents
(prostate cancer; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT Carcinoma
(prostatic; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 475631-20-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(del 103method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 219996-17-5P 219996-19-7P 219996-48-2P 226969-54-6P
226969-85-3P 408501-95-1P 408501-96-2P 408501-97-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 865-21-4D, Vinblastine, oligopeptide conjugates 23214-92-8D, Doxorubicin, oligopeptide conjugates 174640-78-9 174640-79-0
174640-80-3 174640-81-4 174640-82-5 174640-83-6 174640-84-7
174640-85-8 174640-86-9 174640-87-0 174640-88-1 174640-89-2
174640-90-5 174640-91-6 174640-92-7 174640-93-8 189510-06-3
189510-13-2 207401-71-6 219996-18-6 219996-20-0
226969-57-9 226969-59-1 226969-66-0 226969-75-1 226969-77-3
226970-16-7 226970-26-9 408502-10-3 408502-11-4 408502-12-5
408502-14-7 408502-15-8 408502-17-0 408502-18-1 408502-19-2
475631-19-7 475631-21-1 475631-22-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 143-67-9, Vinblastine sulfate 1148-11-4 1676-75-1 24306-54-5
24424-99-5, Di(tert-butyl) dicarbonate 25316-40-9, Doxorubicin hydrochloride 37577-28-9, (1S,2R)-(+)-Norephedrine 103321-52-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 3352-69-0P, 4-Des-Acetylvinblastine 55383-37-4P 113322-99-9P
219996-49-3P 219996-50-6P 219996-51-7P 219996-53-9DP, resin-bound
219996-55-1DP, resin-bound 226969-80-8DP, resin-bound 226969-83-1P
243127-36-8P 408502-26-1DP, resin-bound 408502-27-2P 408502-28-3DP, resin-bound 408502-29-4P 475631-16-4DP, resin-bound 475631-17-5P
475631-18-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 476404-77-0 476404-78-1 476404-79-2 476404-80-5 476404-81-6
476404-82-7 476404-83-8 476404-84-9 476404-85-0 476404-86-1
476404-87-2 476404-88-3 476404-89-4

RL: PRP (Properties)
(unclaimed protein sequence; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

IT 174639-48-6 174639-56-6 174639-60-2 174639-73-7 174639-87-3
174640-46-1 174640-54-1 174640-55-2 174640-56-3 174640-57-4
174640-77-8 189508-82-5 305326-07-2 476370-93-1 476370-94-2
476370-95-3 476370-96-4
RL: PRP (Properties)
(unclaimed sequence; method of treating cancer using conjugate of oligopeptide that is selectively cleaved by PSA and a cytotoxic agent in combination with radiation therapy)

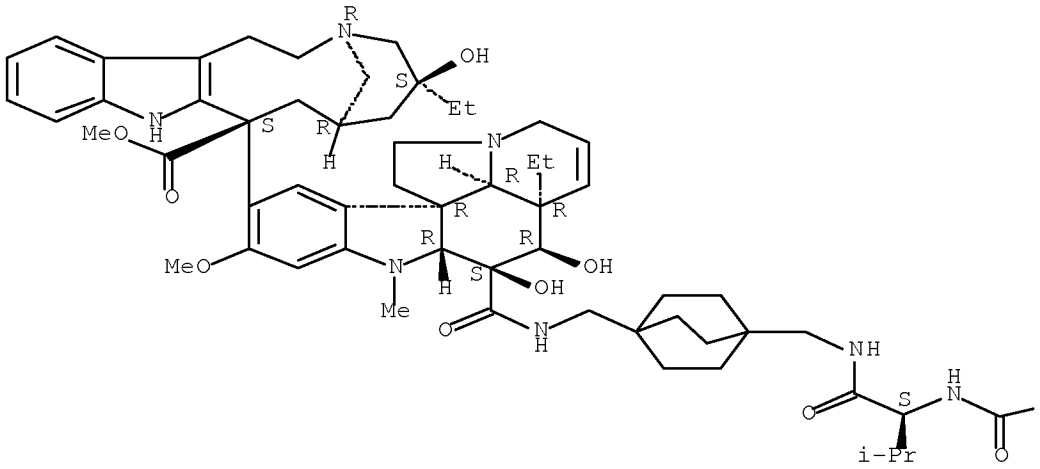
L76 ANSWER 40 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:276519 HCAPLUS Full-text
DOCUMENT NUMBER: 136:310188
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and an NSAID compound
INVENTOR(S): Heimbrook, David C.; Yao, Siu-long
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 129 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20020042375	A1	20020411	US 2001-896245		20010629
PRIORITY APPLN. INFO.:			US 2000-216217P	P	20000705

OTHER SOURCE(S): MARPAT 136:310188
AB The invention relates to methods of treating cancer using a combination of a compound which is a PSA conjugate and a nonsteroidal antiinflammatory agent (NSAID) and to methods of preparing such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) and COX-2 inhibitor 3-phenyl-4-[4-(4-methylsulfonyl)phenyl]-2(5H)furanone is an example of an NSAID compound (syntheses given).
IT 219996-17-5P 219996-18-6P 219996-20-0P
408501-99-5P 408502-00-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
RN 219996-17-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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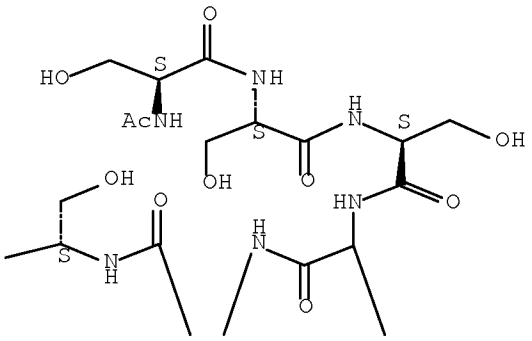


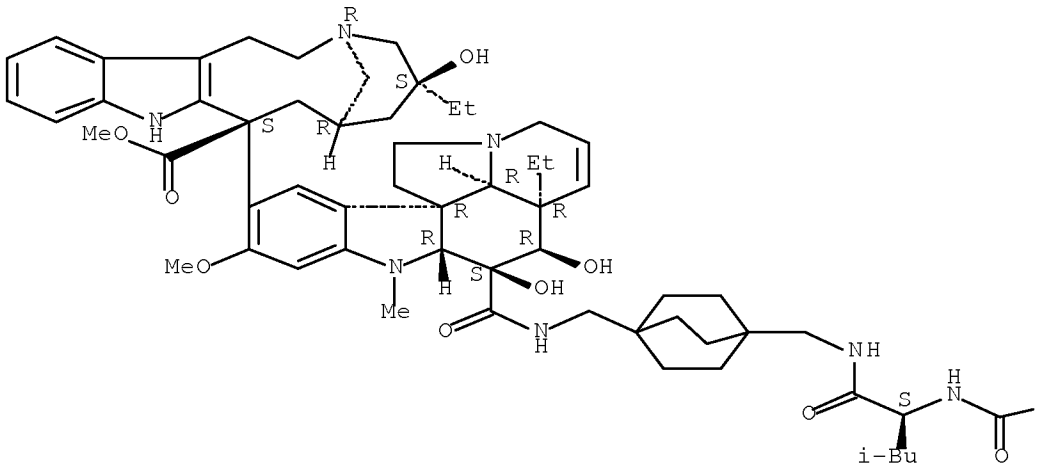
PAGE 2-B

RN 219996-18-6 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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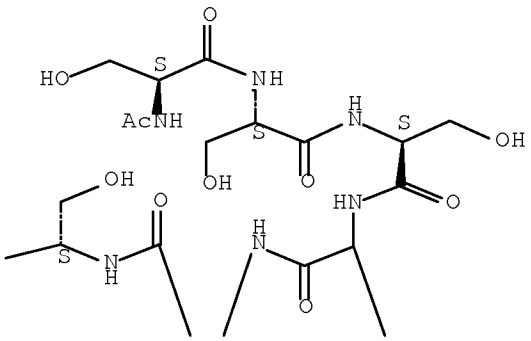
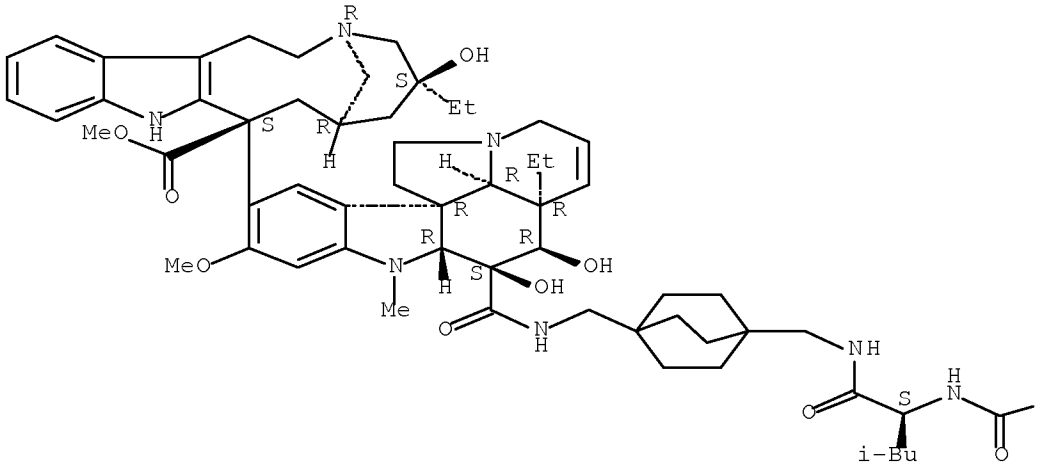


PAGE 2-B

RN 219996-20-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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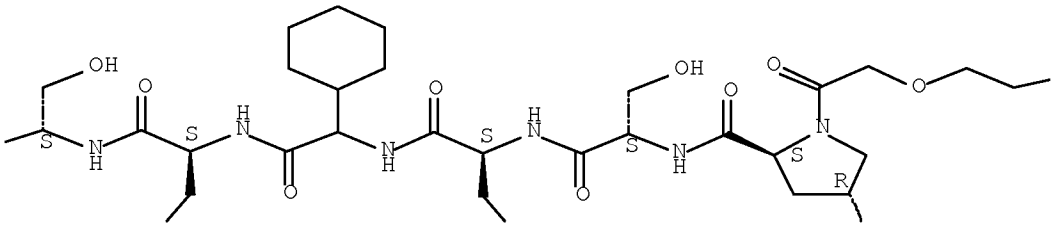

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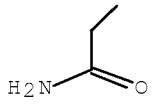
PAGE 2-B



RN 408501-99-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

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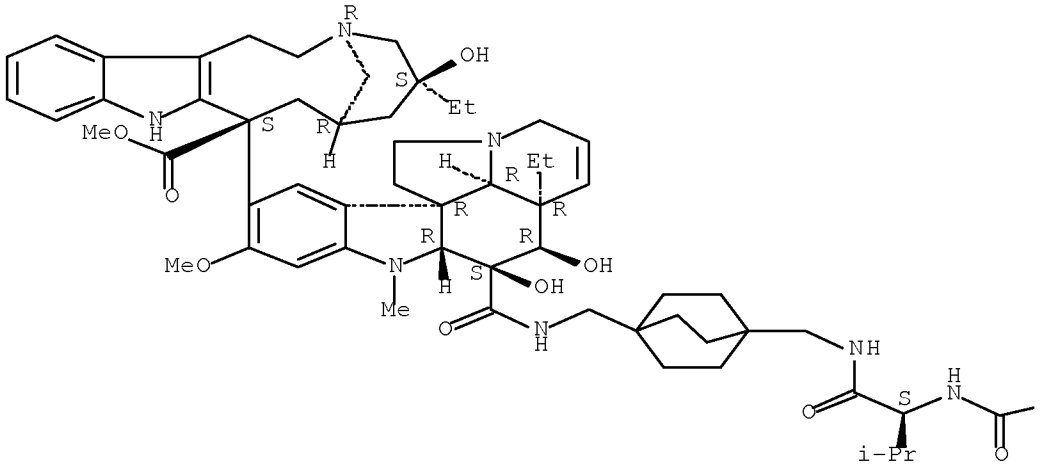
CRN 219996-17-5
CMF C85 H124 N14 O20

Absolute stereochemistry.

PAGE 1-A



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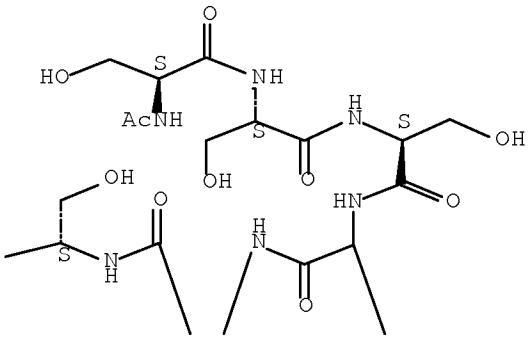
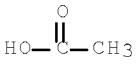


PAGE 2-B

CM 2

CRN 64-19-7
CMF C2 H4 O2



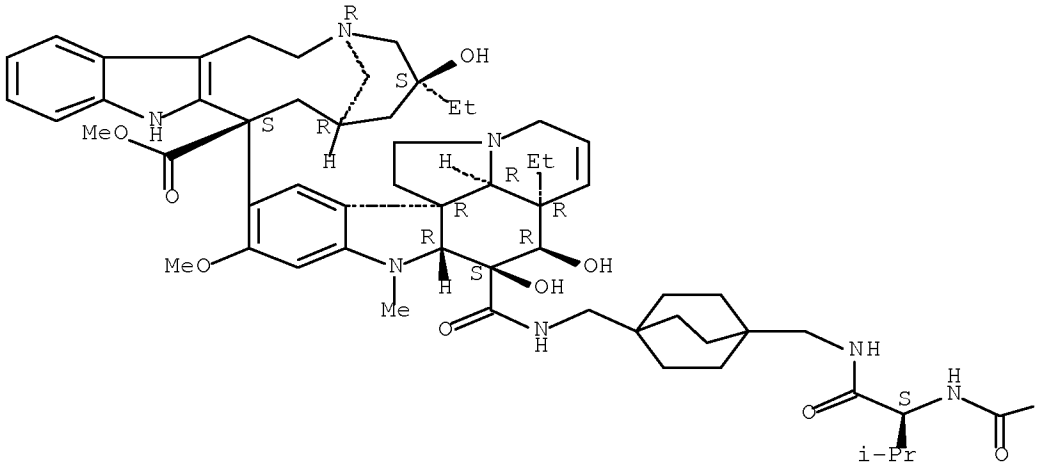
RN 408502-00-1 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 219996-19-7
CMF C92 H136 N14 O23

Absolute stereochemistry.

PAGE 1-A



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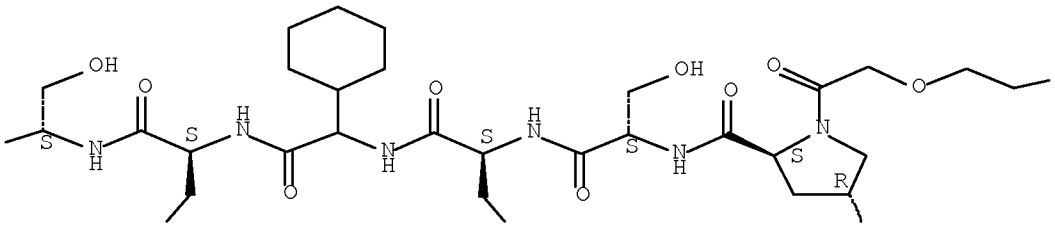

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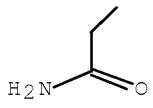
PAGE 2-B



CM 2

CRN 64-19-7
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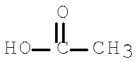

IC ICM A61K038-08
ICS A61K031-444; A61K031-415; A61K031-365; A61K031-454
INCL 514016000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
IT Anti-inflammatory agents
(nonsteroidal; treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
IT Drug delivery systems
(prodrugs; treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
IT Antitumor agents
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
IT Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)
IT 162011-86-1P 162011-90-7P 162012-07-9P 169590-42-5P 174640-78-9P
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181695-72-7P 189510-06-3P 189510-13-2P 189954-13-0P 189954-14-1P
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408502-11-4P 408502-12-5P 408502-13-6P 408502-14-7P 408502-15-8P
408502-16-9P 408502-17-0P 408502-18-1P 408502-19-2P 409098-87-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)

IT 68-12-2, Dmf, reactions 79-11-8, Chloroacetic acid, reactions
103-82-2, Phenylacetic acid, reactions 104-95-0, 4-Bromothioanisole
105-36-2, Ethyl bromoacetate 874-87-3, 4-Methylthiobenzyl chloride
1676-75-1 5470-70-2 25316-40-9, Doxorubicin hydrochloride
37577-28-9, + Norephedrine 55383-37-4 221615-73-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)

IT 23782-85-6P 36437-19-1P, Chloromalonaldehyde 91497-39-1P 98546-51-1P
117037-25-9P 131139-84-9P 162012-30-8P 178619-02-8P 178619-03-9P
219996-51-7P 219996-52-8P 219996-53-9P 221615-71-0P 221615-72-1P
221615-75-4P 226969-80-8P 226969-83-1P 243127-36-8P 243127-40-4P
243127-43-7P 243127-46-0P 243127-55-1P 243127-56-2P 243127-57-3P
243127-58-4P 249561-98-6P 408502-26-1DP, resin-bound 408502-27-2P
408502-28-3DP, resin-bound 408502-28-3P 408502-29-4P 408502-30-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)

IT 53-86-1, Indomethacin 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac
22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Dolobid
36322-90-4 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8,
Nabumetone 71125-38-7, Meloxicam 80937-31-1, Flosulide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)

L76 ANSWER 41 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:276430 HCAPLUS Full-text
DOCUMENT NUMBER: 136:310187
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis
INVENTOR(S): Defeo-Jones, Deborah; Heimbrook, David C.; Jones, Raymond E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 102 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 20020041880	A1	20020411	US 2001-896251	20010629
PRIORITY APPLN. INFO.:			US 2000-215934P P	20000705
OTHER SOURCE(S):	MARPAT 136:310187			

AB The invention relates to methods of treating cancer using a combination of a compound which is a PSA conjugate and a compound which is an inhibitor of angiogenesis and to methods of preparing such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agents. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) and 3-(3-thienyl)-6-(4-methoxyphenyl)pyrazolo[1,5-a]pyrimidine is an example of an angiogenesis inhibitor (syntheses given).

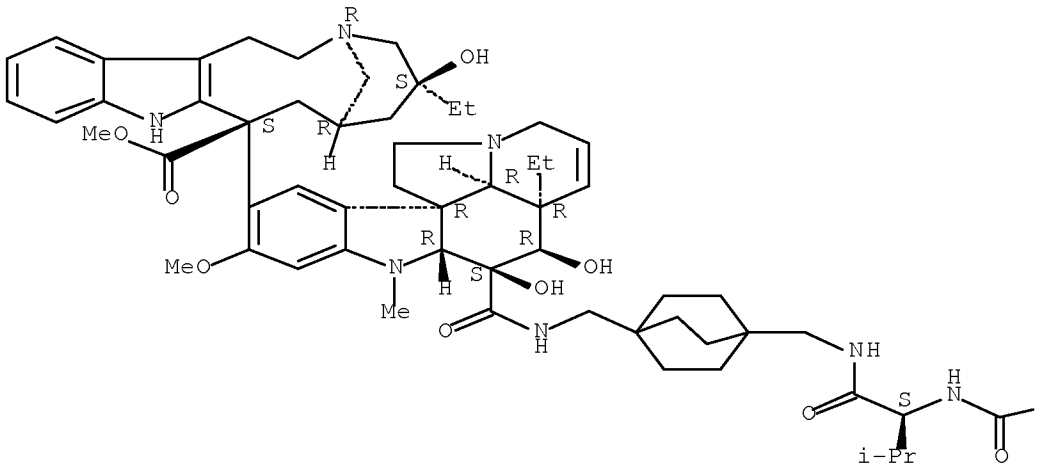
IT 219996-17-5P 219996-18-6P 219996-19-7P
219996-20-0P 408501-99-5P 408502-00-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)

RN 219996-17-5 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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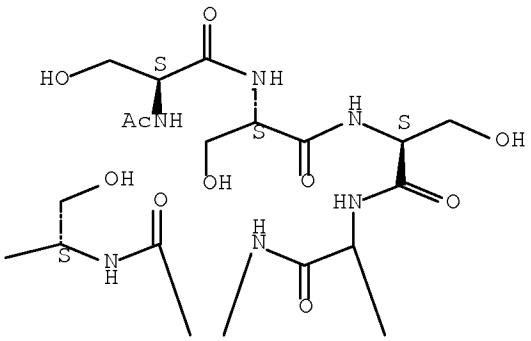
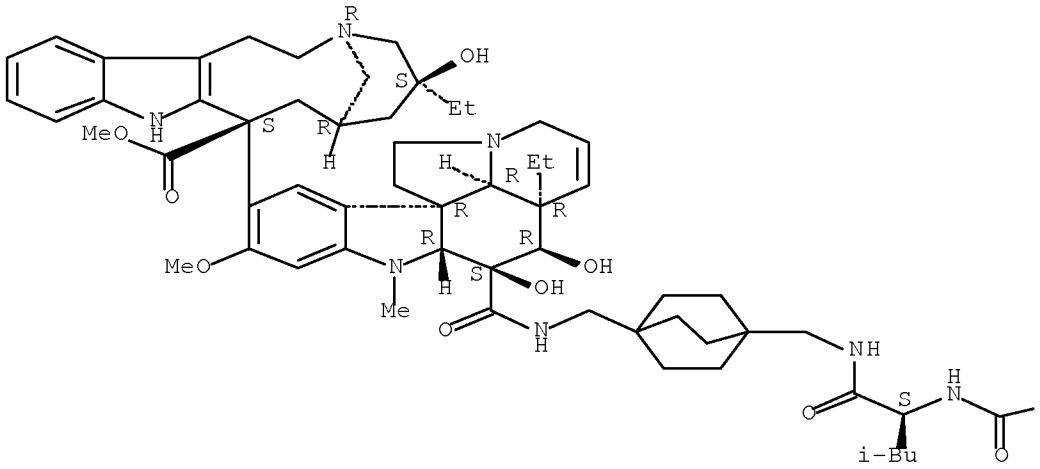


PAGE 2-B

RN 219996-18-6 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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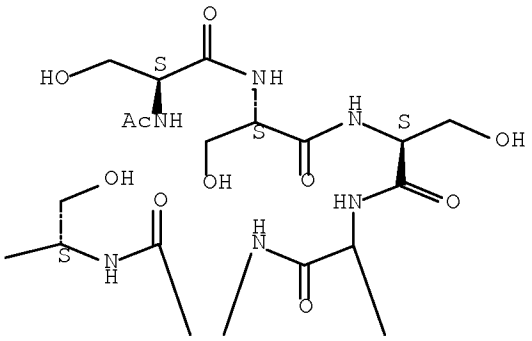


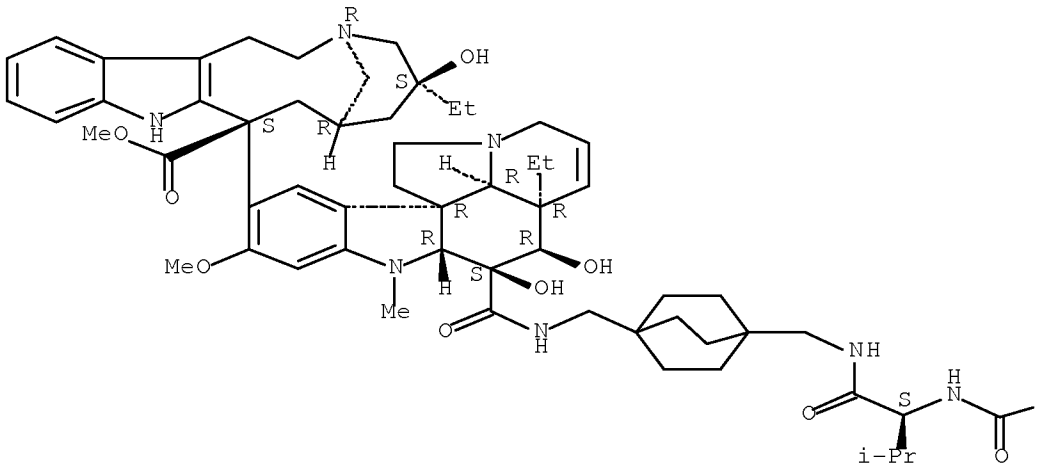
PAGE 2-B

RN 219996-19-7 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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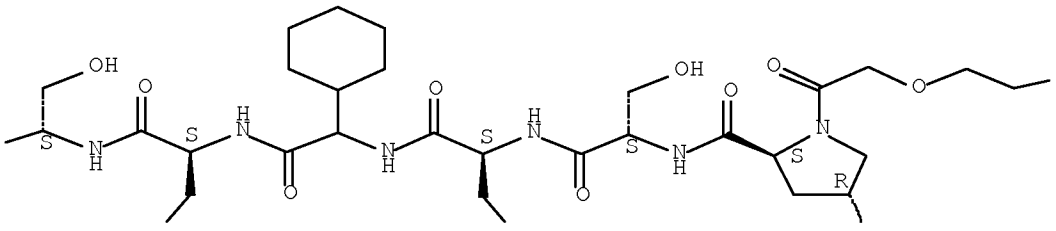

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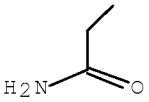
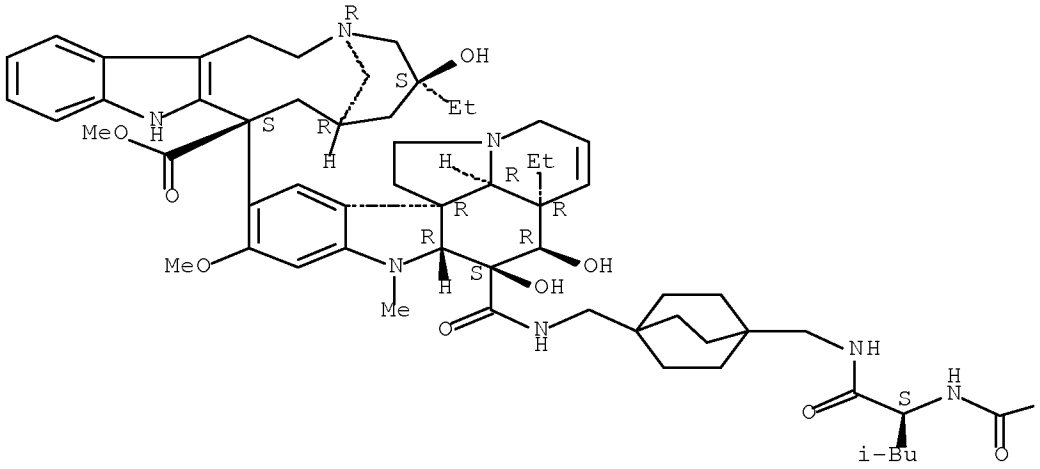
PAGE 2-B



RN 219996-20-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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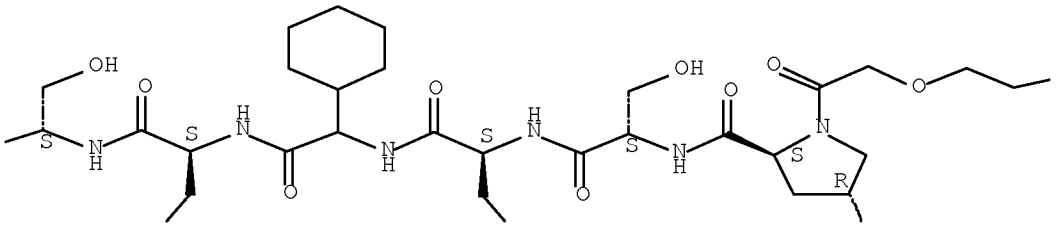

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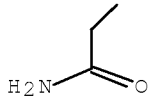
PAGE 2-B



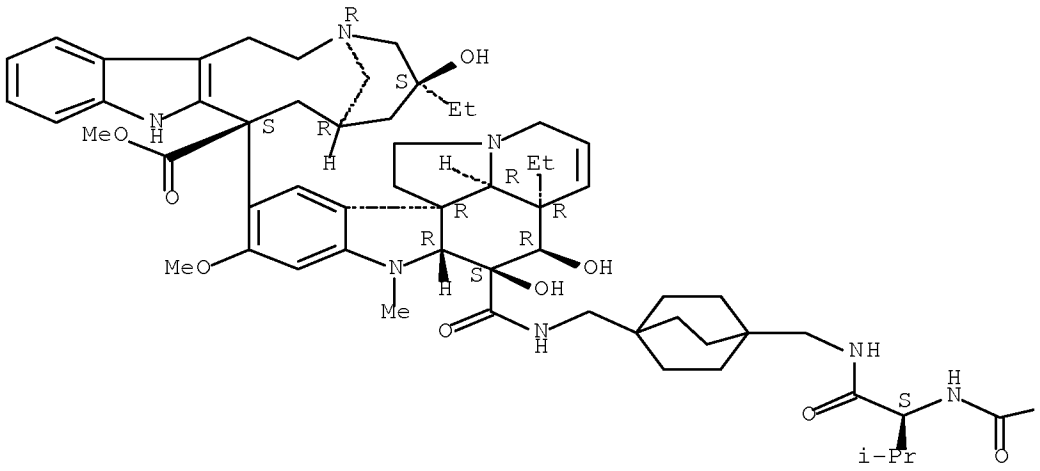
RN 408501-99-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 219996-17-5
CMF C85 H124 N14 O20

Absolute stereochemistry.

PAGE 1-A



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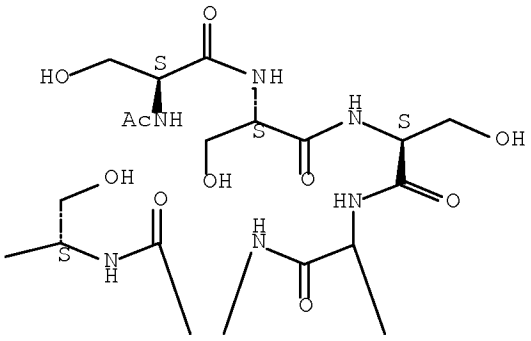
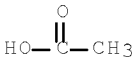


PAGE 2-B

CM 2

CRN 64-19-7
CMF C2 H4 O2



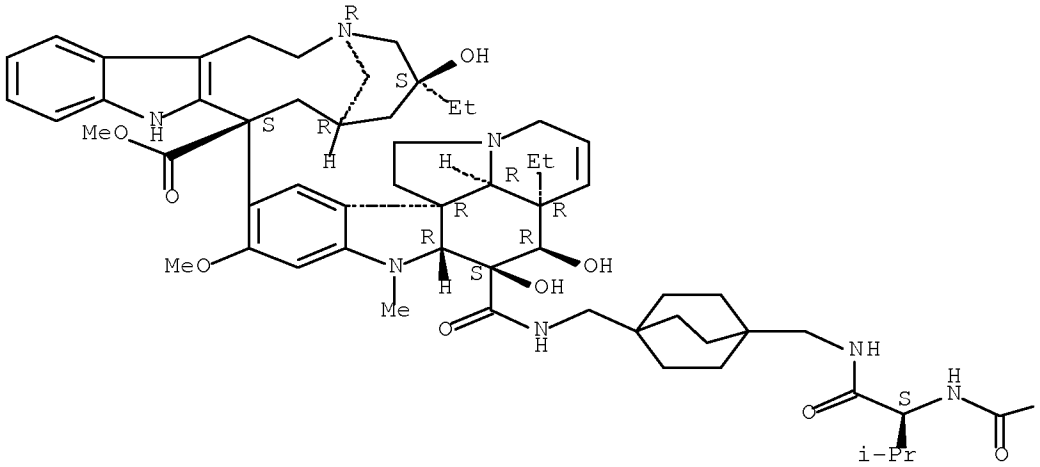
RN 408502-00-1 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 219996-19-7
CMF C92 H136 N14 O23

Absolute stereochemistry.

PAGE 1-A



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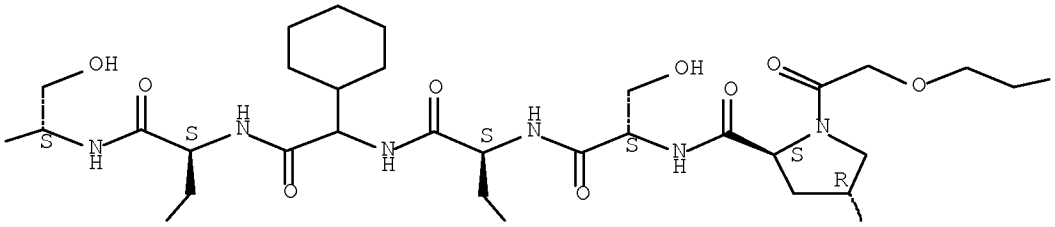

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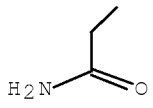
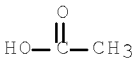
PAGE 2-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



IC ICM A61K039-00
ICS A61K038-14; A61K038-08
INCL 424185100
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
IT Drug delivery systems
(prodrugs; treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)
IT Angiogenesis
Antitumor agents
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)
IT Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)
IT 216661-57-3P 216661-79-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)
IT 174640-78-9P 174640-79-0P 174640-80-3P 174640-81-4P 174640-82-5P
174640-84-7P 174640-85-8P 174640-86-9P 174640-87-0P 174640-88-1P
174640-89-2P 174640-90-5P 174640-91-6P 174640-92-7P 174640-93-8P
189510-06-3P 189510-13-2P 216661-42-6P 216661-44-8P 216661-45-9P
216661-46-0P 216661-48-2P 216661-49-3P 216661-50-6P 216661-51-7P
216661-53-9P 216661-54-0P 216661-55-1P 216661-58-4P 216661-59-5P
216661-60-8P 216661-61-9P 216661-63-1P 216661-64-2P 216661-65-3P
216661-66-4P 216661-68-6P 216661-70-0P 216661-72-2P 216661-76-6P
216661-80-2P 216661-82-4P 216661-83-5P 216661-84-6P 216661-85-7P
216661-86-8P 219996-17-5P 219996-18-6P
219996-19-7P 219996-20-0P 226969-54-6P 226969-57-9P
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226969-75-1P 226969-77-3P 226969-85-3P 226970-16-7P 226970-26-9P
243127-50-6P 243127-53-9P 293298-44-9P 293298-45-0P 293298-46-1P
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335649-69-9P 335649-70-2P 335649-71-3P 335649-72-4P 335649-74-6P
357187-08-7P 357187-09-8P 357187-10-1P 357187-11-2P 357187-12-3P
357187-13-4P 357187-14-5P 357187-19-0P 408501-94-0P 408501-95-1P
408501-96-2P 408501-97-3P 408501-99-5P 408502-00-1P
408502-01-2P 408502-02-3P 408502-03-4P 408502-04-5P 408502-05-6P
408502-06-7P 408502-07-8P 408502-08-9P 408502-09-0P 408502-10-3P

408502-11-4P 408502-12-5P 408502-13-6P 408502-14-7P 408502-15-8P
408502-16-9P 408502-17-0P 408502-18-1P 408502-19-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)

IT 104-16-5 1148-11-4 1676-75-1 1953-54-4, 5-Hydroxyindole 2008-75-5
3647-69-6 6165-69-1 7250-67-1 16461-94-2 17288-40-3 20265-39-8
25316-40-9, Doxorubicin hydrochloride 37577-28-9, + Norephedrine
55383-37-4 65192-28-1 73183-34-3 128676-84-6 149246-86-6
408502-21-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)

IT 100367-39-3P 106792-38-5P 117037-25-9P 128676-85-7P 219996-48-2P
219996-51-7P 219996-52-8P 219996-53-9DP, resin-bound 219996-53-9P
219996-55-1P 226969-80-8P 226969-83-1P 243127-36-8P 243127-40-4P
243127-43-7P 243127-46-0P 243127-55-1P 243127-56-2P 243127-57-3P
243127-58-4P 335649-60-0P 335649-61-1P 335649-62-2P 335649-63-3P
357187-15-6P 357187-16-7P 408502-22-7P 408502-23-8P 408502-24-9P
408502-26-1DP, resin-bound 408502-27-2P 408502-28-3DP, resin-bound
408502-28-3P 408502-29-4P 408502-30-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)

IT 408502-25-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(treatment of cancer with a prostate specific antigen (PSA) conjugate and an inhibitor of angiogenesis)

L76 ANSWER 42 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:850971 HCAPLUS Full-text
DOCUMENT NUMBER: 136:4721
TITLE: Human polypeptides causing or leading to the killing of cells including lymphoid tumor cells
INVENTOR(S): Nagy, Zoltan; Brunner, Christoph; Tesar, Michael; Thomassen-Wolf, Elisabeth
PATENT ASSIGNEE(S): GPC Biotech A.-G., Germany; Morphosys A.-G.
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087337	A1	20011122	WO 2001-US15625	20010514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156060	A1	20011121	EP 2000-110065	20000512

EP 1156060	B1	20070627			
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CA 2408360	A1	20011122	CA 2001-2408360		20010514
EP 1289551	A1	20030312	EP 2001-935513		20010514
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CN 1607959	A	20050420	CN 2001-809346		20010514
AU 2001261602	B2	20060706	AU 2001-261602		20010514
US 20030032782	A1	20030213	US 2001-1934		20011115
AU 2006225244	A1	20061026	AU 2006-225244		20061005
PRIORITY APPLN. INFO.:			EP 2000-110065	A	20000512
			US 2000-238492P	P	20001006
			WO 2001-US15625	W	20010514

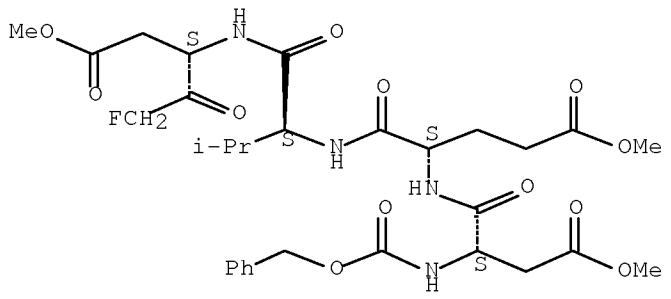
AB The present invention relates to polypeptide compns. which bind to cell surface epitopes and, in multivalent forms, cause or lead to the killing of cells including lymphoid tumor cells, and in the case of monovalent forms, cause immunosuppression or otherwise inhibit activation of lymphocytes. The invention further relates to nucleic acids encoding the polypeptides, methods for the production of the polypeptides, methods for killing cells, methods for immunosuppressing a patient, pharmaceutical, diagnostic and multivalent compns. and kits comprising the polypeptides and uses of the polypeptides.

IT 210344-95-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K039-395
ICS A61K039-44

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63

ST Ig heavy light chain lymphoid tumor; surface antigen MHC I II HLADR

IT Animal cell line
(B cell lymphoblastoid; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Lymphoblast

(B-cell, cell line; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Lymphoma
(B-cell; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(BJAB; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(BONNA-12; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Lymphoma
(Burkitt's; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(DOHH-2; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(EOL-1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(GRANTA-519; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(HC-1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(HD-MY-Z; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(HDLM-2; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DP; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DQ; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR1, DR1-0101; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR2, DR2-15021; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR3, DR3-0301; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HLA-DR4, DR4Dw4-0401 and DR4Dw10-0402; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR6, DR6-1302 and DR6-1401; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR8, DR8-8031; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR9, DR9-9012; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DR; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DRw52, B3*0101; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DRw53B4*0101; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgA; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG2a; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG2b; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG3; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG4; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgM; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(KARPAS-299; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(KARPAS-422; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(KM-H2; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(L-363; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(L-428; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(L1236; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(LP-1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), class II; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex); multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(MHH-CALL-4; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(MHH-PREB-1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(MN-60; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(NALM-1; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(Priess; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(RPMI-8226; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Animal cell line
(Raji; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(SR-786; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Animal cell line
(SR-7; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Cell proliferation
(T cell, inhibition; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Lymphoma
(T-cell; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Lymphocyte
(activation; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Inflammation
Spinal column, disease
(ankylosing spondylitis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Autoimmune disease
Inflammation
Thyroid gland, disease
(autoimmune thyroiditis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Biology
Pharmaceutical industry
(business; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Drug delivery systems
(carriers; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Polymers, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cross-linked; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Inflammation
Kidney, disease
(glomerulonephritis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Transplant and Transplantation
(graft-vs.-host reaction; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chain; multivalent polypeptides comprising antibody-based

antigen-binding domain for killing lymphoid tumor cells)
IT Intestine, disease
(inflammatory; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Apoptosis
(innate; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Autoimmune disease
(insulin-dependent diabetes mellitus; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Diabetes mellitus
(insulin-dependent; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Inflammation
Pancreatic islet of Langerhans, disease
(insulitis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Rheumatoid arthritis
(juvenile; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chain; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Cell proliferation
(lymphocyte, suppression; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Cell activation
(lymphocyte; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Myeloid leukemia
(multiple; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Acute B-cell leukemia
Acute myeloid leukemia
Animals
Chronic lymphocytic leukemia
Chronic myeloid leukemia
Cytotoxic agents
DNA sequences
Diagnostic agents
Epitopes
Genetic vectors
Graves' disease
Hairy cell leukemia
Hodgkin's disease
Immune disease
Immunosuppressants
Immunosuppression
Labels
Lymphocyte
Lymphoma
Molecular cloning
Multiple sclerosis
Myasthenia gravis
Narcolepsy

Protein sequences
Psoriasis
Rheumatoid arthritis
Sjogren syndrome
Test kits
Transplant rejection
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antigens
Nucleic acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Peptides, biological studies
Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multivalent; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Inflammation
Pancreas, disease
(pancreatitis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Skin, disease
(pemphigus vulgaris; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Biliary tract, disease
(primary biliary cirrhosis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT T cell (lymphocyte)
(proliferation, inhibition; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Lymphocyte
(proliferation, suppression; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Disease, animal
(proliferative, cell; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Interleukin 2
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(secretion inhibition; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface; multivalent polypeptides comprising antibody-based

antigen-binding domain for killing lymphoid tumor cells)
IT Lupus erythematosus
(systemic; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT Inflammation
Thyroid gland, disease
(thyroiditis; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 375398-98-4P 375398-99-5P 375399-08-9P 375399-09-0P 375399-12-5P 375399-13-6P 375399-15-8P 375399-24-9P 375399-25-0P 375399-26-1P 375399-27-2P 375399-28-3P 375399-29-4P 375399-30-7P 376414-45-8P 376414-46-9P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 210344-95-9 220644-02-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 375372-62-6 375372-64-8 375372-66-0 376355-12-3 376595-71-0 376595-78-7 376595-79-8
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(non-caspase; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 374744-00-0P, DNA (synthetic plasmid pMORPH13-scFv) 374744-01-1P, DNA (synthetic plasmid pMx7-FS-5D2) 374744-02-2P, DNA (synthetic plasmid pMx9-Fab-GPC-8) 375398-97-3P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; multivalent polypeptides comprising antibody-based antigen-binding domain for killing lymphoid tumor cells)
IT 280106-91-4 374573-78-1 374573-79-2 374573-80-5 374573-81-6 374573-82-7 374573-83-8 374573-84-9 374573-85-0 374573-86-1 374573-87-2 374587-75-4 375372-59-1 375372-60-4 375372-61-5 375372-63-7 375372-65-9 376355-13-4 376355-14-5 376355-15-6 376355-16-7 376355-17-8 376355-18-9 376424-57-6
RL: PRP (Properties)
(unclaimed sequence; human polypeptides causing or leading to the killing of cells including lymphoid tumor cells)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 43 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:487157 HCAPLUS Full-text
DOCUMENT NUMBER: 136:226380
TITLE: Treatment with inhibitors of caspases, that are substrates of drug transporters, selectively permits chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells
AUTHOR(S): Blagosklonny, M. V.
CORPORATE SOURCE: Medicine Branch, National Cancer Institute, NIH, Bethesda, MD, 20892, USA

SOURCE: Leukemia (2001), 15(6), 936-941
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

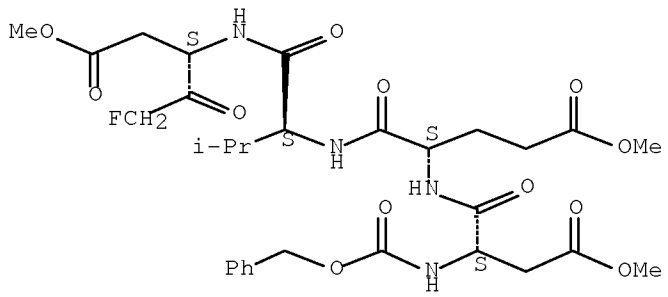
AB Many chemotherapeutic agents induce apoptosis in tumor cells, but killing of normal cells remains a major obstacle. Development of multidrug resistance further limits chemotherapy in cancer. Here, I show that multidrug resistance can be exploited for selective killing of multidrug-resistant cells by a combination of an apoptosis-inducing agent that is not a substrate of either Pgp or MRP (eg flavopiridol) with a caspase inhibitor that is a substrate (eg Z-DEVD-fmk). In normal cells, treatment with caspase inhibitors prevented PARP cleavage, nuclear fragmentation, and cell death caused by flavopiridol or epothilone B. In contrast, Pgp- and MRP-expressing cells were not rescued by caspase inhibitors. Furthermore, reversal of drug resistance renders Pgp cells sensitive to caspase inhibitors abolishing therapeutic advantage. Thus, caspase inhibitors, that are inactive in multidrug-resistant cells, protect normal but not multidrug-resistant cells against chemotherapy, permitting selective eradication of multidrug-resistant cells. Clin. application of this approach may diminish the toxic side-effects of chemotherapy in patients with multidrug-resistant tumors.

IT 210344-95-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

RN 210344-95-9 HCAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 1-6 (Pharmacology)

IT 146426-40-6, Flavopiridol 152044-54-7, Epothilone B 210344-95-9 220644-02-0 220760-26-9 220760-27-0 220760-28-1 325786-54-7 403601-94-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

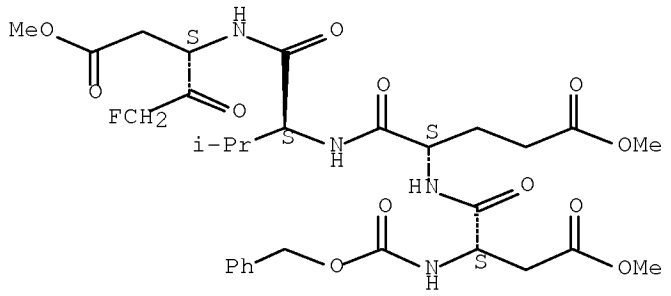
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 44 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:91508 HCAPLUS Full-text
DOCUMENT NUMBER: 134:131819
TITLE: Preparation of dipeptide apoptosis inhibitors
INVENTOR(S): Keana, John F. W.; Cai, Sui Xiong; Guastella, John; Yang, Wu; Drewe, John A.
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 168,945, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184210	B1	20010206	US 1999-270736	19990316
US 6596693	B1	20030722	US 2000-653279	20000831
US 20030181391	A1	20030925	US 2003-429095	20030505
US 6949516	B2	20050927		
US 20050192231	A1	20050901	US 2005-100470	20050407

PRIORITY APPLN. INFO.: US 1997-61676P P 19971010
US 1998-168945 B2 19981009
US 1999-270736 A3 19990316
US 2000-653279 A3 20000831
US 2003-429095 A3 20030505
OTHER SOURCE(S): MARPAT 134:131819
AB Dipeptides R1-AA-NHCH(CH2CO2R3)COCH2F (R1 is an N-terminal protecting group selected from Boc, Ac, or Cbz; R3 is alkyl or H; AA is a residue of an amino acid selected from Val, Ile or Leu) were prepared as apoptosis inhibitors. Thus, Cbz-Val-Asp-fmk (fmk = fluoromethyl ketone), prepared by reaction of 2-fluoroethanol with tert-Bu 3-nitropropanoate, nitro group reduction of tert-Bu 5-fluoro-4-hydroxy-3-nitropentanoate, coupling with Cbz-Valine, Dess-Martin oxidation and trifluoroacetic acid-catalyzed ester cleavage, was assayed for apoptosis inhibitory activity in several examples (IC50 = 0.04 μM for inhibition of caspase-3).
IT 210344-95-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of dipeptide apoptosis inhibitors)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K038-05
ICS C07K004-00
INCL 514019000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT DNA
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of dipeptide apoptosis inhibitors)
IT 153088-73-4 187389-52-2 187389-53-3 210344-95-9
210344-98-2 321690-65-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of dipeptide apoptosis inhibitors)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 45 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:725653 HCAPLUS Full-text
DOCUMENT NUMBER: 133:296450
TITLE: Preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer.
INVENTOR(S): Defeo-Jones, Deborah; Jones, Raymond E.; Oliff, Allen I.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 544 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059930	A1	20001012	WO 2000-US8762	20000331

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 20030220241 A1 20031127 US 2002-244215 20020916
PRIORITY APPLN. INFO.: US 1999-127746P P 19990405
US 2000-542769 A1 20000404

OTHER SOURCE(S): MARPAT 133:296450

AB A method for achieving a therapeutic effect in a mammal comprises administration of ≥1 inhibitor of prenyl protein transferase and ≥1 prostate specific antigen conjugate. Thus, mice injected s.c. with LNCaP.FGC cells were treated with 2-4 μM 1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone hydrochloride (preparation given) and with 7.5 mg/kg [N-glutaryl-(4-trans-L-Hyp)]-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin-3'-yl) over 4 days to give marked tumor shrinkage vs. controls.

IT 301296-27-5P 301297-35-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

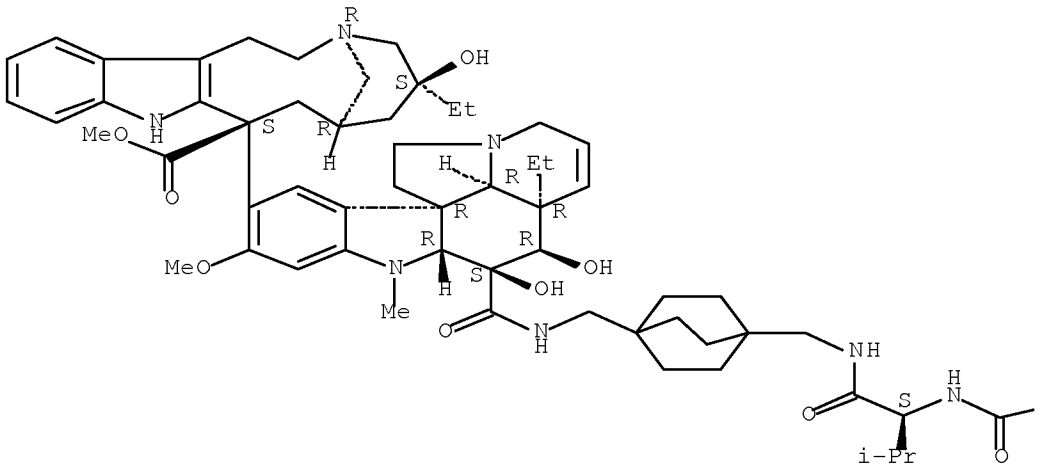
RN 301296-27-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

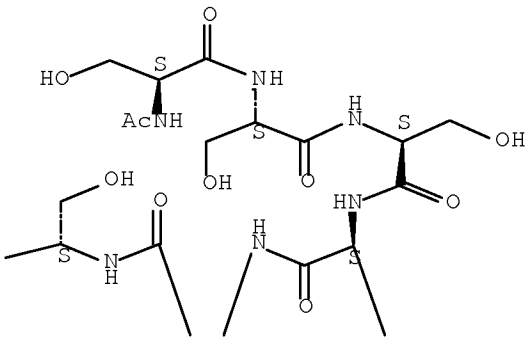
CRN 301296-26-4
CMF C85 H124 N14 O20

Absolute stereochemistry.

PAGE 1-A



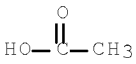
PAGE 1-B



PAGE 2-B

CM 2

CRN 64-19-7
CMF C2 H4 O2



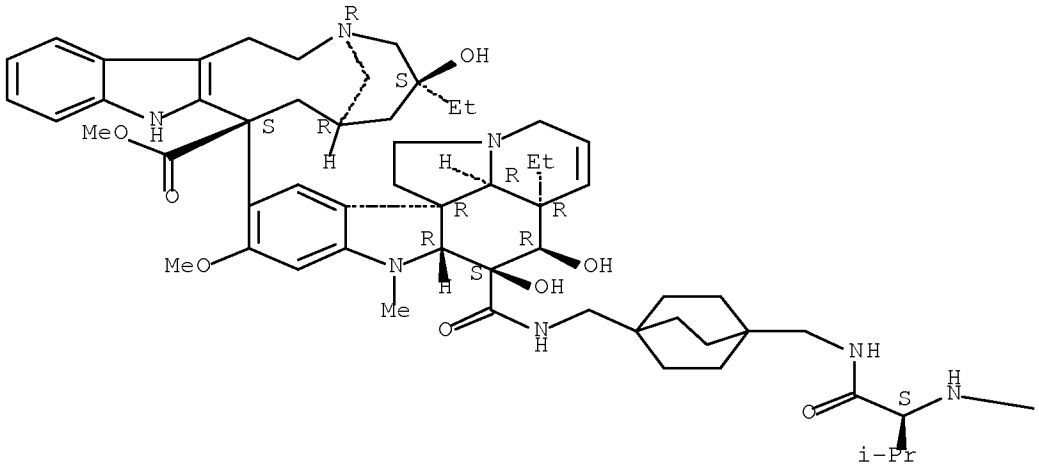
RN 301297-35-8 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

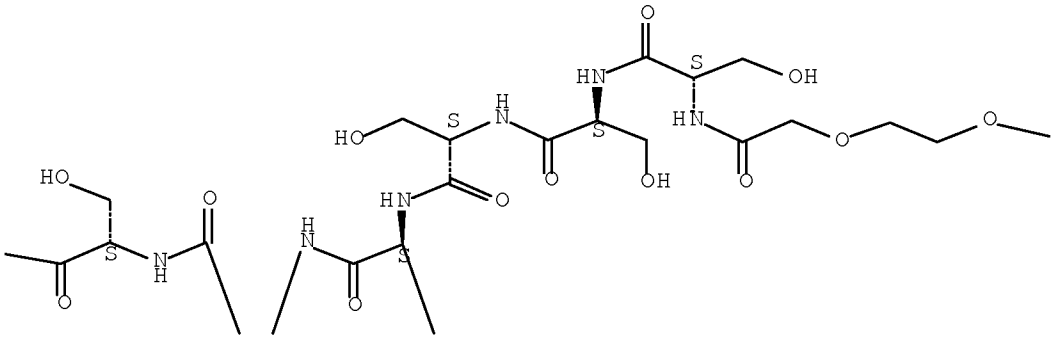
CRN 301297-34-7
CMF C90 H134 N14 O23

Absolute stereochemistry.

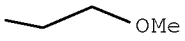
PAGE 1-A



PAGE 1-B



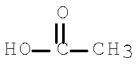
PAGE 1-C



PAGE 2-B

CM 2

CRN 64-19-7
CMF C2 H4 O2



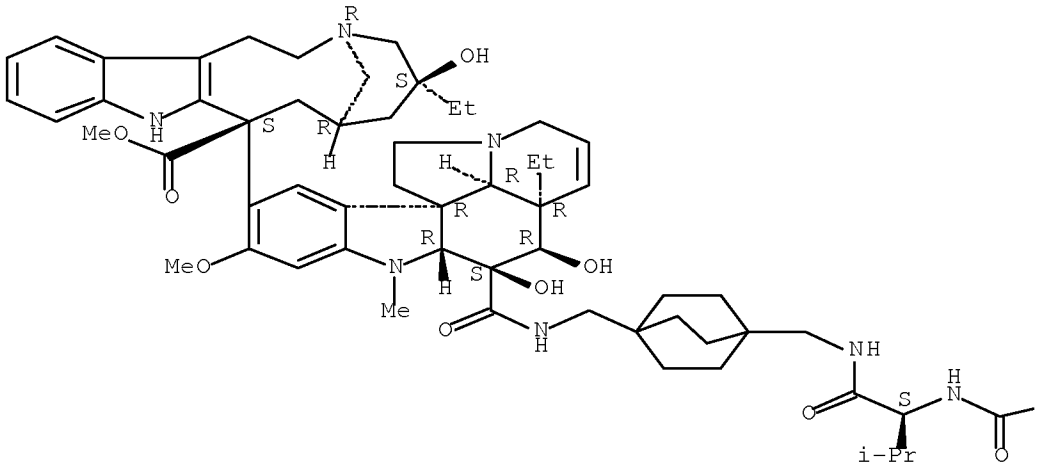
IT 301296-26-4 301296-52-6 301296-53-7
301296-54-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

RN 301296-26-4 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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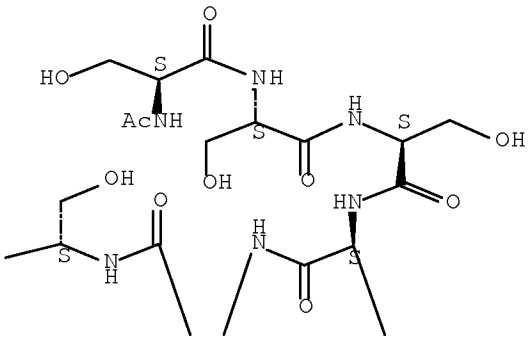


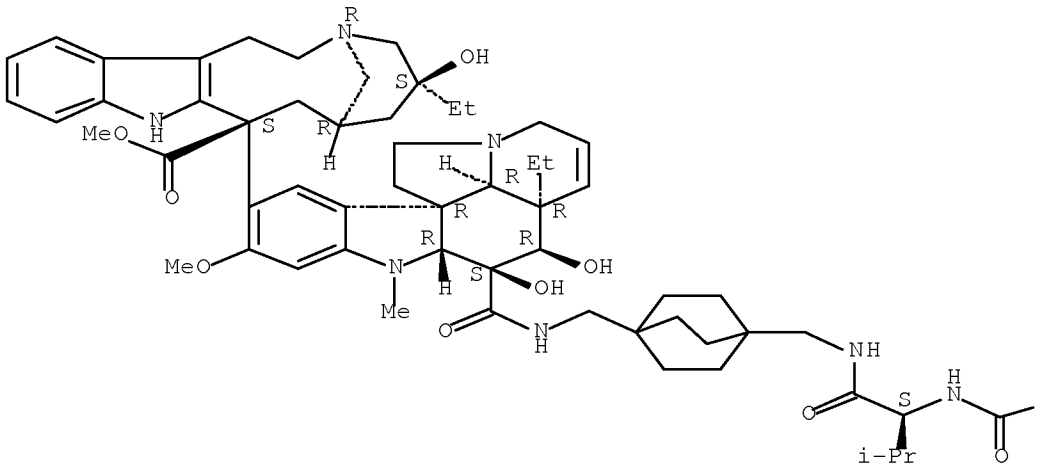
PAGE 2-B

RN 301296-52-6 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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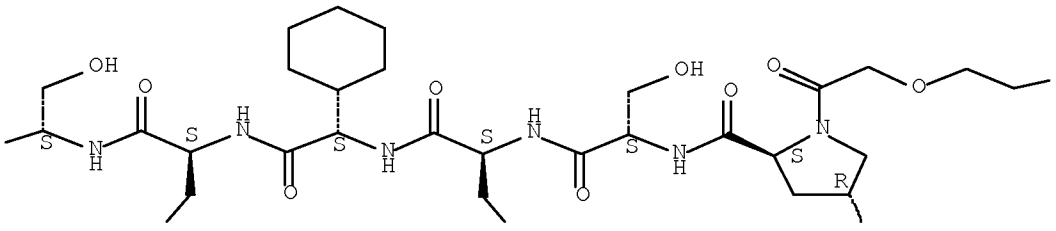
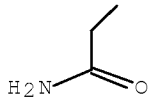


PAGE 1-C

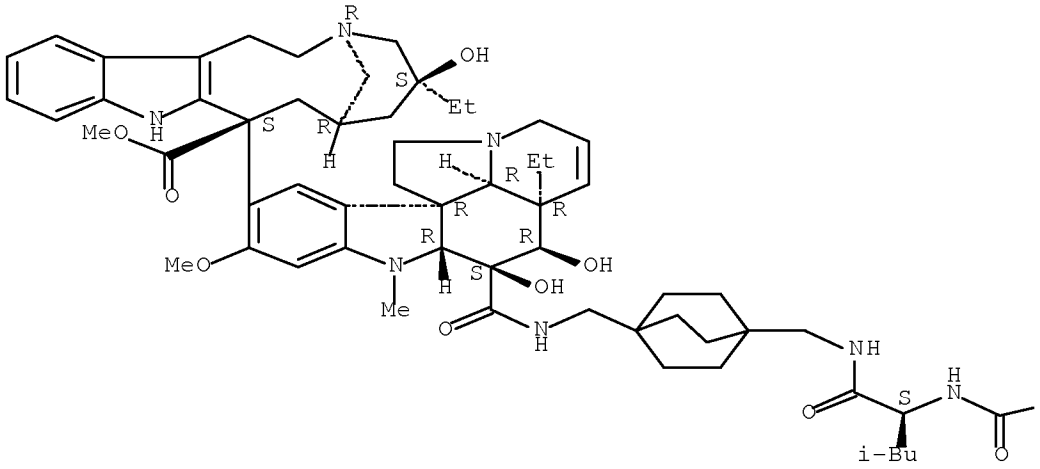
PAGE 2-B



RN 301296-53-7 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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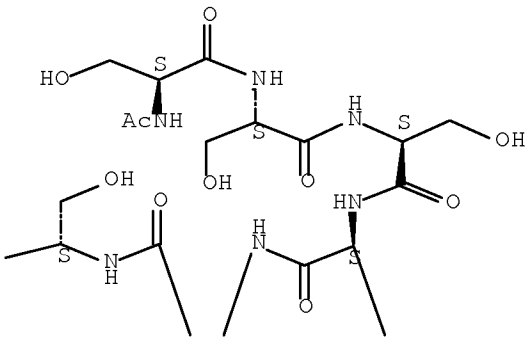
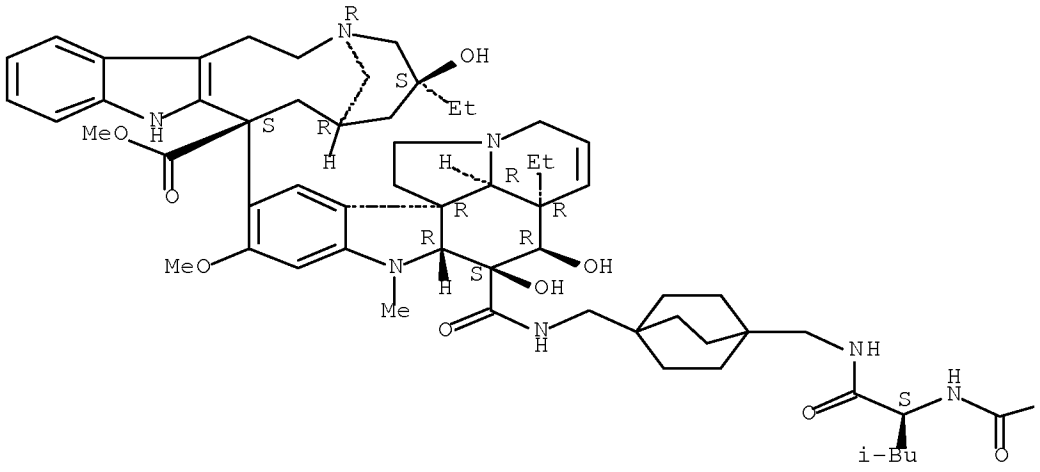


PAGE 2-B

RN 301296-54-8 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-(2S)-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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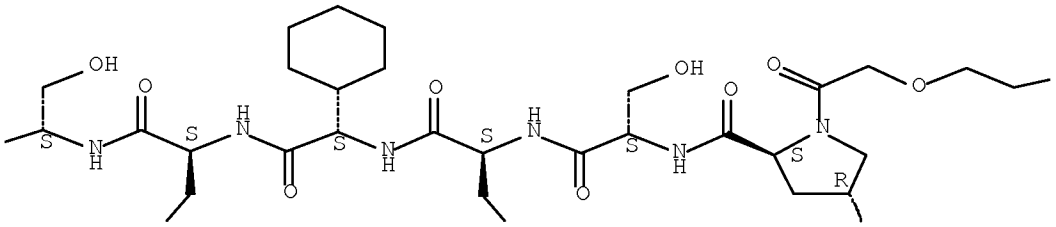

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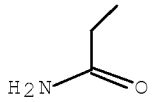
PAGE 2-B



IC ICM C07K005-09
ICS A61K038-00; A61K031-495; A61K031-55
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 31, 34
ST prenyl protein transferase inhibitor prostate specific antigen conjugate anticancer; cancer prostate treatment PSA conjugate prenyl protein transferase inhibitor; doxorubicin PSA conjugate prepn prostate cancer treatment; vinblastine PSA conjugate prepn prostate cancer treatment; chlorophenylcyanobenzylimidazolylmethylpiperazinone prepn prostate cancer treatment
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-Ha-ras; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-Ki-ras; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Peptides, preparation
Prostate-specific antigen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of

prostate cancer)
IT Ras proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(farnesylation; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Prostate gland
Prostate gland
(neoplasm, inhibitors; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Transformation, neoplastic
(oncogene-transformed, inhibition; preparation of prenyl protein transferase
inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Plasmids
(pDSE100, construction; preparation of prenyl protein transferase inhibitors
and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Plasmid vectors
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer
)
IT Antitumor agents
(prostate gland; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
IT Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(v-Ha-ras; preparation of prenyl protein transferase inhibitors and prostate
specific antigen conjugates for combination treatment of prostate cancer)
IT Alkaloids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(vinca, peptide conjugates; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)
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RL: PRPH (Prophetic)
(Preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer.)
IT 9001-78-9, Alkaline phosphatase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SEAP; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

IT 131384-38-8, Farnesyl protein transferase 135371-29-8, Geranylgeranyl protein transferase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer
)

IT 75-16-1, Methylmagnesium bromide 79-04-9, Chloroacetyl chloride
108-42-9, 3-Chloroaniline 135-19-3, 2-Naphthol, reactions 141-43-5, reactions 142-08-5, 2-Hydroxypyridine 288-32-4, Imidazole, reactions
452-74-4, 4-Bromo-3-fluorotoluene 540-51-2 619-44-3, Methyl 4-iodobenzoate 1122-41-4, 2,4-Dichlorothiophenol 3510-66-5, 2-Bromo-5-methylpyridine 4214-79-3, 5-Chloro-2-pyridinol 10408-29-4, 2-Methoxymandelic acid 17201-43-3, α-Bromo-p-tolunitrile
18113-03-6, 2-Chloro-4-methoxyphenol 22282-72-0 25316-40-9, Doxorubicin hydrochloride 31166-44-6, Benzyl 1-piperazinecarboxylate
37577-28-9 53957-33-8 55383-37-4 67935-17-5 71556-74-6
186202-42-6 191544-97-5 205186-83-0 207395-79-7 207395-90-2
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

IT 15996-76-6P, 4-Cyanobenzylamine hydrochloride 18282-51-4P, 4-Iodobenzyl alcohol 101048-76-4P, 2-Fluoro-4-formylbenzonitrile 117037-25-9P
127838-40-8P 127838-58-8P 153556-42-4P, 4-Bromo-3-fluorobenzoic acid
169503-35-9P 179626-27-8P 183500-36-9P,
1-(4-Cyanobenzyl)-5-hydroxymethylimidazole 183500-94-9P 197856-23-8P,
1-(4-Cyanobenzyl)-5-chloromethylimidazole hydrochloride 210037-17-5P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of prenyl protein transferase inhibitors and prostate specific antigen conjugates for combination treatment of prostate cancer)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 46 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:628177 HCAPLUS Full-text
DOCUMENT NUMBER: 133:208197
TITLE: Preparation of low molecular weight peptide derivatives as inhibitors of the laminin/nidogen interaction
INVENTOR(S): Stilz, Hans Ulrich; Gerl, Martin; Flynn, Gary A.; Stankova, Magda; Binnie, Robert A.
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052051	A1	20000908	WO 2000-EP1386	20000219
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TR 200102560	T2	20020121	TR 2001-2560		20000219
BR 2000008647	A	20020122	BR 2000-8647		20000219
HU 2002000192	A2	20020629	HU 2002-192		20000219
HU 2002000192	A3	20020930			
ZA 2001006972	A	20020807	ZA 2001-6972		20000219
JP 2002539092	T	20021119	JP 2000-602275		20000219
AU 779779	B2	20050210	AU 2000-31577		20000219
RU 2262509	C2	20051020	RU 2001-126403		20000219
CN 1237075	C	20060118	CN 2000-804501		20000219
CN 1775801	A	20060524	CN 2005-10124755		20000219
AT 370969	T	20070915	AT 2000-909221		20000219
EP 1845106	A1	20071017	EP 2007-13872		20000219
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
ES 2288844	T3	20080201	ES 2000-909221		20000219
US 6365572	B1	20020402	US 2000-517123		20000229
IN 2001CN01142	A	20050304	IN 2001-CN1142		20010813
MX 2001008337	A	20020108	MX 2001-8337		20010817
HK 1042499	A1	20060714	HK 2002-104064		20020531
PRIORITY APPLN. INFO.:			EP 1999-103869	A	19990301
			CN 2000-804501	A3	20000219
			EP 2000-909221	A3	20000219
			WO 2000-EP1386	W	20000219

OTHER SOURCE(S): MARPAT 133:208197

AB Peptides R1-X-NHCH[(CH2)nCONH2]CONHCHR2COR3 [R1 is an acyl group; X is -NR4CHR5CO-, where R4 and R5 taken together form a heterocyclic ring containing D [(CH2)r, O, S, NH, NR, (CH2)rO, (CH2)rS, (CH2)rNH, (CH2)rNR, where R = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, or aryl and r = 0-3] and substituted by R or R-Y [Y = O, S, iminocarbonyl, or (CH2)r], NHCH(D-R)CO, or NHCHR-D-CO; R2 = H, alkyl, -E-OH, E-CO2H, E-CONH2, where E is an (un)substituted alkyl chain; R3 = substituted 1-pyrrolidinyl or piperidino, NH, NHCO2H, NHCONH2, NHCH2OH, etc.; n = 1 or 2] were prepared as inhibitors of the laminin/nidogen interaction. Thus, succinyl-L-3-(2-naphthyl)alanyl-L-asparaginyl-L-seryl- L-valylglycine 3-hydroxypropylamide, prepared by peptide coupling in solution, showed IC50 = 0.36 and 0.09 μM in the HTS and 3-day equilibrium assay, resp.

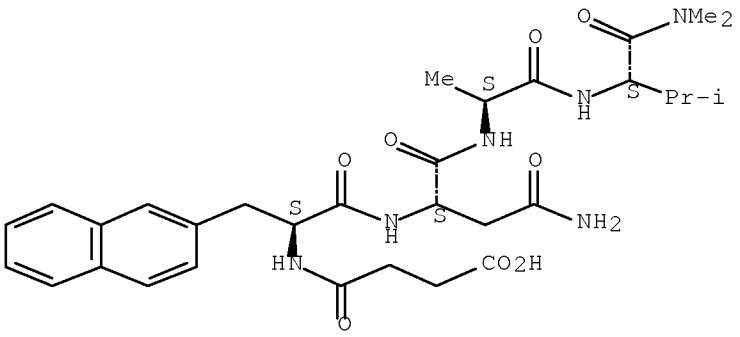
IT 290369-82-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of low mol. weight peptide derivs. as inhibitors of the laminin/nidogen interaction)

RN 290369-82-3 HCAPLUS

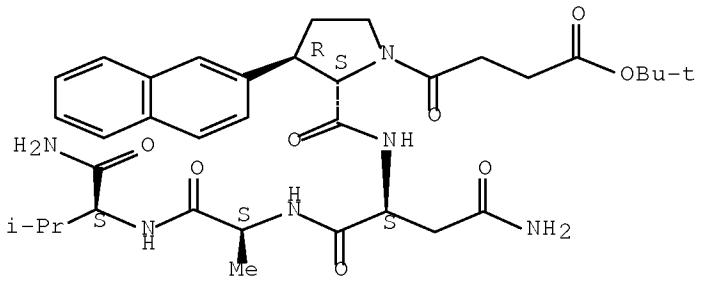
CN L-Valinamide, N-(3-carboxy-1-oxopropyl)-3-(2-naphthalenyl)-L-alanyl-L-asparaginyl-L-alanyl-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 290369-87-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of low mol. weight peptide derivs. as inhibitors of the laminin/nidogen interaction)
RN 290369-87-8 HCAPLUS
CN L-Valinamide, (3R)-1-[4-(1,1-dimethylethoxy)-1,4-dioxobutyl]-3-(2-naphthalenyl)-L-prolyl-L-asparaginyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K014-78
ICS C07K005-10; C07K005-08; A61K038-39; A61P019-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT Blood vessel, neoplasm
(hemangioma; preparation of low mol. weight peptide derivs. as inhibitors of the laminin/nidogen interaction)
IT 290369-41-4P 290369-42-5P 290369-43-6P 290369-44-7P 290369-45-8P
290369-46-9P 290369-47-0P 290369-48-1P 290369-49-2P 290369-50-5P
290369-51-6P 290369-52-7P 290369-53-8P 290369-54-9P 290369-55-0P
290369-56-1P 290369-57-2P 290369-58-3P 290369-59-4P 290369-60-7P
290369-61-8P 290369-62-9P 290369-63-0P 290369-64-1P 290369-65-2P
290369-66-3P 290369-67-4P 290369-68-5P 290369-69-6P 290369-70-9P
290369-71-0P 290369-72-1P 290369-73-2P 290369-74-3P 290369-75-4P
290369-76-5P 290369-77-6P 290369-78-7P 290369-79-8P 290369-80-1P
290369-81-2P 290369-82-3P 290369-83-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of low mol. weight peptide derivs. as inhibitors of the laminin/nidogen interaction)

IT 14734-25-9P 15026-17-2P, Butanedioic acid, mono(1,1-dimethylethyl) ester 49711-14-0P 82954-58-3P 114833-06-6P 282531-69-5P 282531-70-8P 282531-71-9P 282531-72-0P 282531-73-1P 290369-84-5P 290369-85-6P 290369-86-7P 290369-87-8P 290369-89-0P 290369-90-3P 290369-91-4P 290369-92-5P 290369-93-6P 290369-94-7P 290369-95-8P 290369-96-9P 290369-97-0P 290369-98-1P 290369-99-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of low mol. weight peptide derivs. as inhibitors of the laminin/nidogen interaction)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 47 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:241263 HCAPLUS Full-text
DOCUMENT NUMBER: 132:279548
TITLE: Preparation of tetrapeptide thiomethyl-, aminomethyl-, and sulfonamidomethyl-ketone derivs. as caspase inhibitors useful for treatment of apoptosis
INVENTOR(S): Lee, Dennis
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020440	A1	20000413	WO 1999-US23271	19991006
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1129108	A1	20010905	EP 1999-953073	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003524603	T	20030819	JP 2000-574551	19991006
PRIORITY APPLN. INFO.:			US 1998-103428P P	19981006
			WO 1999-US23271 W	19991006

OTHER SOURCE(S): MARPAT 132:279548
AB This invention discloses novel compds. R1Z-AA1-AA2-AA3-NHCH(CH2CO2H)COCH2XR2 [I; R1 = alkyl, alkylaryl, aryl; Z = CO, SO2, NHCO; AA1, AA2, AA3 = (independently) a naturally occurring amino acid; X = S, O, N; R2 = alkyl, alkylaryl, aryl when X is sulfur or Y-R3 when X is nitrogen; Y = SO2, CO; R3 = (undefined) e.g. Me, Ph], their pharmaceutical compns., and the novel inhibition of caspases (no data) for use in the treatment of apoptosis, and disease states caused by excessive or inappropriate cell death. Thus, H2NCH(CH2CO2Bu-t)CHOHCH2N3 (preparation given) was coupled to tripeptide Ac-Asp(OBu-t)-Glu(OBu-t)-Val-OH to give the tetrapeptide azidomethyl alc. The azidomethyl alc. was reduced to the aminomethyl alc. and reacted benzoyl chloride to give Ac-Asp(OBu-t)-Glu(OBu-t)-Val-NHCH(CH2CO2Bu-t)CHOHCH2NHCOPh which was oxidized to the ketone and deprotected with TFA to give Ac-Asp-Glu-Val-NHCH(CH2CO2H)COCH2NHCOPh. Representative compds. of formula I were said to inhibit caspase 3 in vitro.

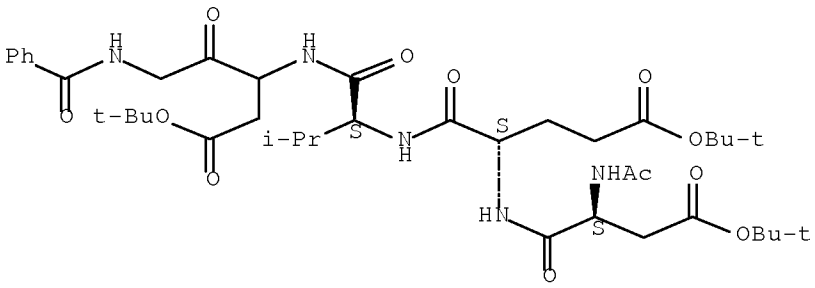
IT 263859-21-8P 263859-23-0P 263859-25-2P 263859-28-5P 263859-31-0P 263859-34-3P 263859-36-5P 263859-37-6P 263859-38-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tetrapeptide thiomethyl-, aminomethyl-, and sulfonamidomethyl-ketone derivs. as caspase inhibitors useful for treatment of apoptosis)

RN 263859-21-8 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[3-(benzoylamino)-1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxopropyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

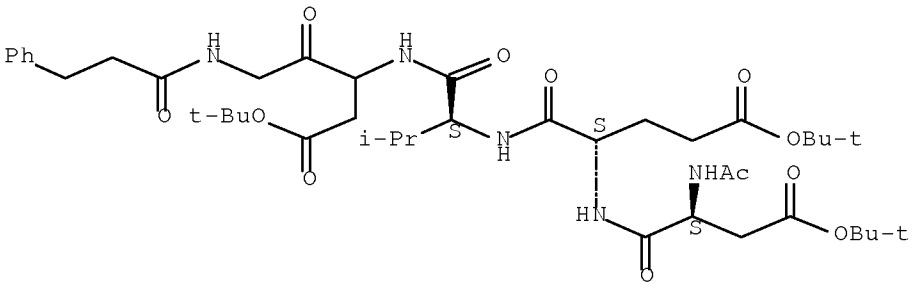
Absolute stereochemistry.



RN 263859-23-0 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxo-3-[(1-oxo-3-phenylpropyl)amino]propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

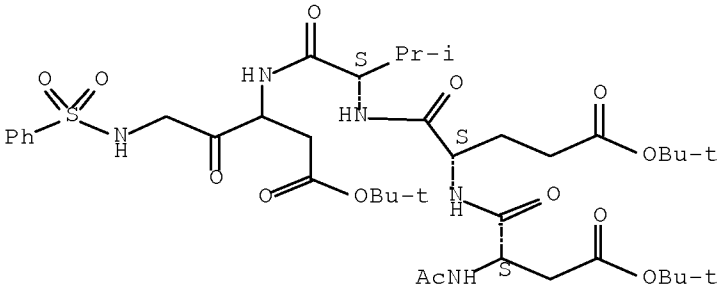
Absolute stereochemistry.



RN 263859-25-2 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxo-3-[(phenylsulfonyl)amino]propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

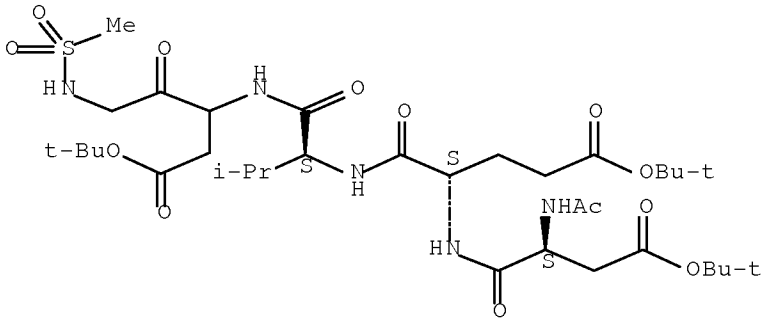
Absolute stereochemistry.



RN 263859-28-5 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3-[(methylsulfonyl)amino]-2-oxopropyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

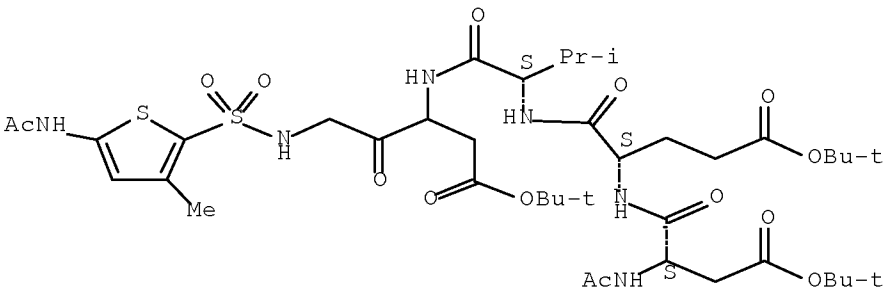
Absolute stereochemistry.



RN 263859-31-0 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[3-[[[5-(acetylamino)-3-methyl-2-thienyl]sulfonyl]amino]-1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxopropyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

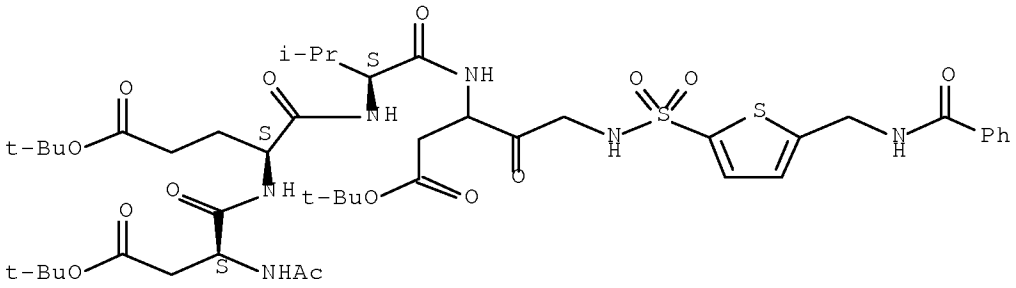
Absolute stereochemistry.



RN 263859-34-3 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[3-[[[5-[(benzoylamino)methyl]-2-thienyl]sulfonyl]amino]-1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxopropyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

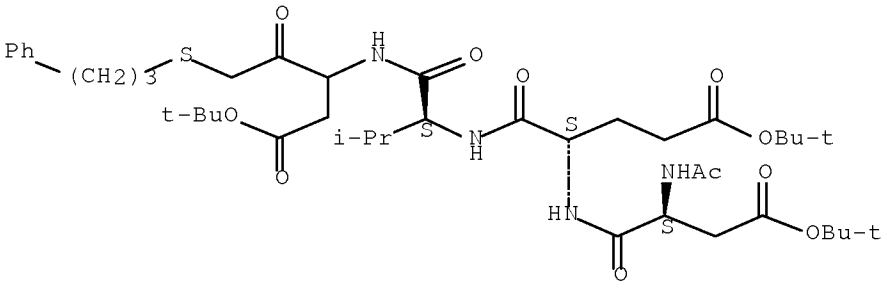
Absolute stereochemistry.



RN 263859-36-5 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxo-3-[(3-phenylpropyl)thio]propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

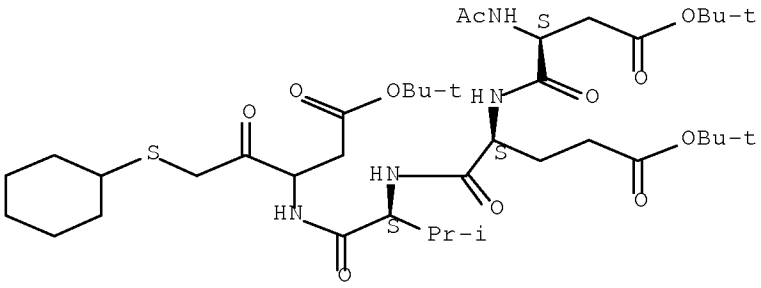
Absolute stereochemistry.



RN 263859-37-6 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[3-(cyclohexylthio)-1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxopropyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

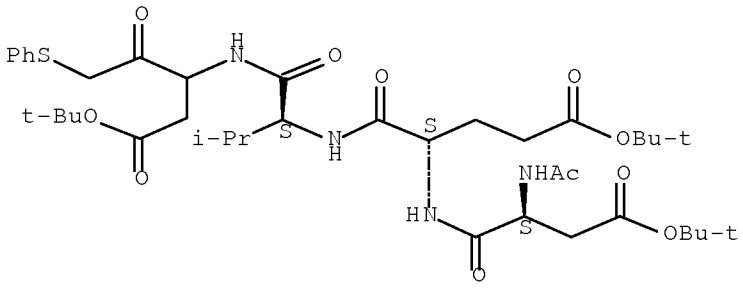
Absolute stereochemistry.



RN 263859-38-7 HCAPLUS

CN L-Valinamide, N-acetyl-L-α-aspartyl-L-α-glutamyl-N-[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-2-oxo-3-(phenylthio)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K005-08

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST peptide methyl ketone prepn inhibitor caspase treatment apoptosis; interleukin 1 beta inhibitor tetrapeptide methylketone prepn; tumor necrosis factor prodn blocking tetrapeptide methylketone prepn

IT Interleukin 1β
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(blocking of production; preparation of tetrapeptide thiomethyl-, aminomethyl-,
and sulfonamidomethyl-ketone derivs. as caspase inhibitors useful for treatment of apoptosis)

IT 21760-98-5P 66447-55-0P 138486-76-7P 220328-33-6P 263859-09-2P
263859-10-5P 263859-11-6P 263859-12-7P 263859-13-8P 263859-14-9P
263859-15-0P 263859-16-1P 263859-17-2P 263859-18-3P 263859-19-4P
263859-20-7P 263859-21-8P 263859-22-9P 263859-23-0P
263859-24-1P 263859-25-2P 263859-26-3P 263859-28-5P
263859-30-9P 263859-31-0P 263859-33-2P 263859-34-3P
263859-35-4P 263859-36-5P 263859-37-6P
263859-38-7P 263859-39-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of tetrapeptide thiomethyl-, aminomethyl-, and sulfonamidomethyl-ketone derivs. as caspase inhibitors useful for treatment of apoptosis)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 48 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:64698 HCAPLUS Full-text
DOCUMENT NUMBER: 130:139655
TITLE: Oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer
INVENTOR(S): Brady, Stephen F.; Garsky, Victor M.; Pawluczyk, Joseph M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9902175	A1	19990121	WO 1998-US14413		19980709
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2295860	A1	19990121	CA 1998-2295860		19980709
AU 9883960	A	19990208	AU 1998-83960		19980709
AU 740597	B2	20011108			
EP 1009420	A1	20000621	EP 1998-934444		19980709
EP 1009420	B1	20031217			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
US 6127333	A	20001003	US 1998-112656		19980709
JP 2002510325	T	20020402	JP 1999-509003		19980709
AT 256473	T	20040115	AT 1998-934444		19980709
PRIORITY APPLN. INFO.:			US 1997-52195P	P	19970710
			GB 1998-10183	A	19980513
			WO 1998-US14413	W	19980709

OTHER SOURCE(S): MARPAT 130:139655
AB Chemical conjugates which comprise oligopeptides, having amino acid sequences that are selectively proteolytically cleaved by free prostate-specific antigen (PSA) and known cytotoxic agents are disclosed. The conjugates of the invention are characterized by a diamine linker between the oligopeptide and vinblastine. Such conjugates are useful in the treatment of prostatic cancer and benign prostatic hypertrophy (BPH).
IT 219996-18-6P 219996-20-0P 219996-24-4P
219996-26-6P 219996-27-7P 219996-28-8P
219996-29-9P 219996-30-2P 219996-31-3P
219996-32-4P 219996-33-5P 219996-34-6P
219996-35-7P 219996-36-8P 219996-37-9P
219996-38-0P 219996-39-1P 219996-41-5P
219996-42-6P 219996-43-7P 219996-44-8P
219996-45-9P 219996-46-0P 219996-47-1P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

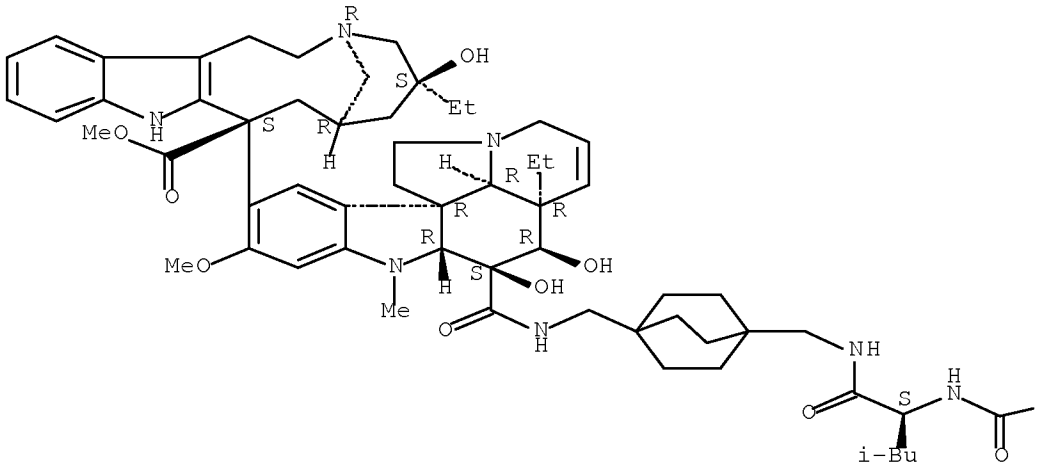
process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

RN 219996-18-6 HCAPLUS

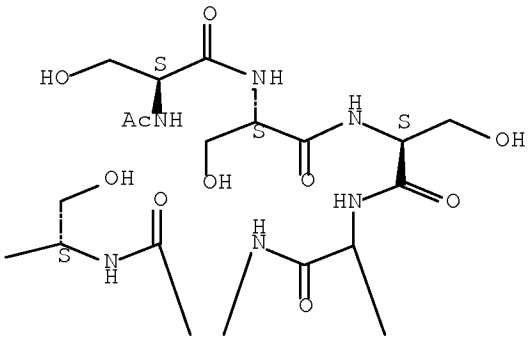
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

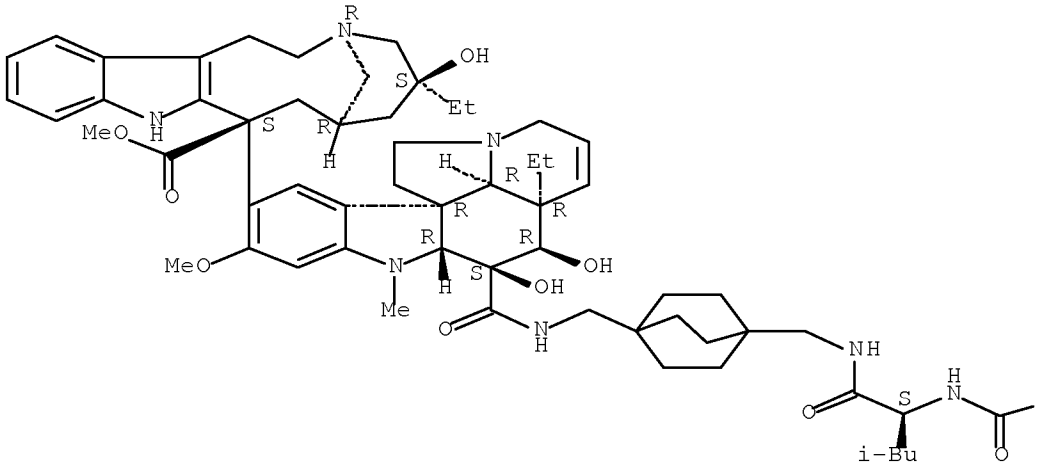


PAGE 2-B

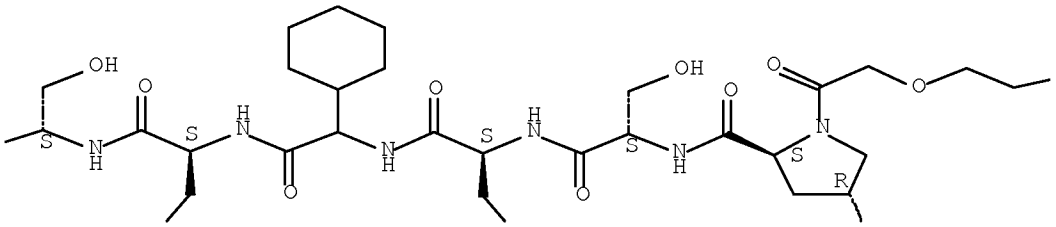
RN 219996-20-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

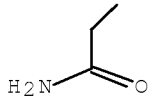


PAGE 1-B



PAGE 1-C

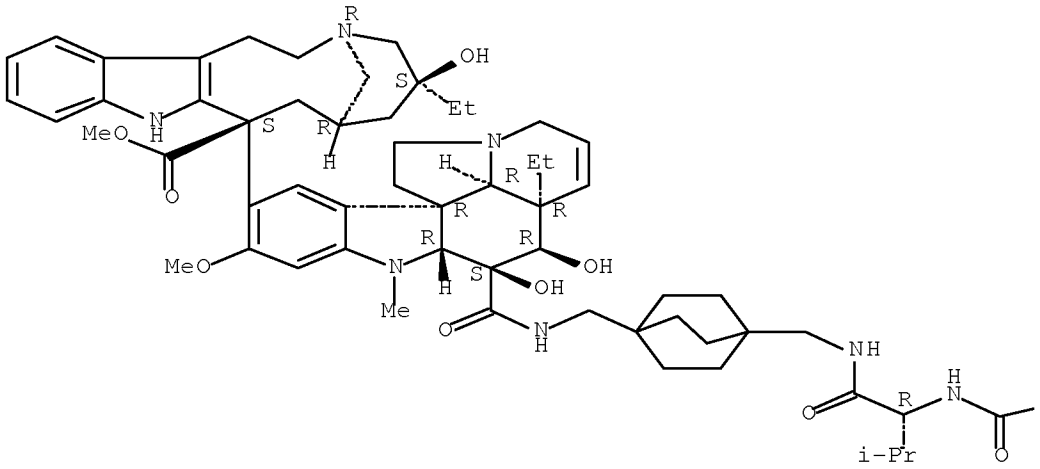
PAGE 2-B



RN 219996-24-4 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-D-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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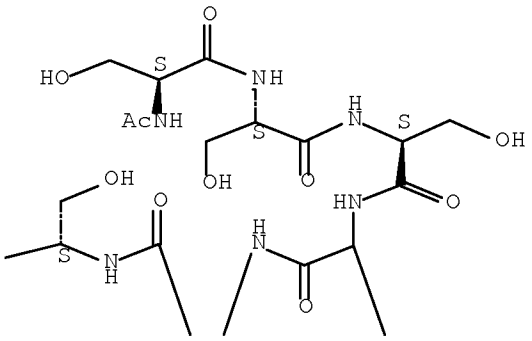


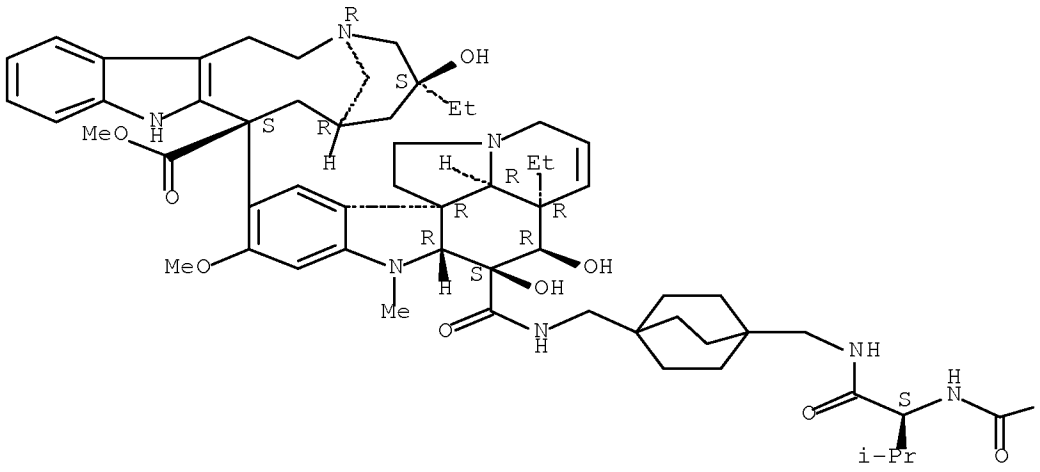
PAGE 2-B

RN 219996-26-6 HCAPLUS

CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 8-amide with hydroxyacetyl-(4R)-4-hydroxy-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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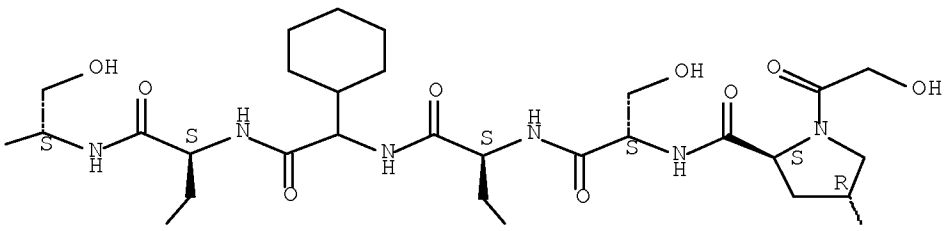
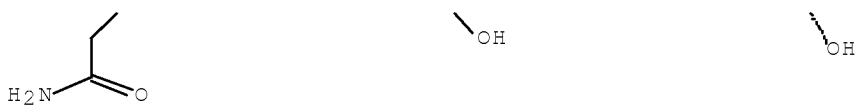


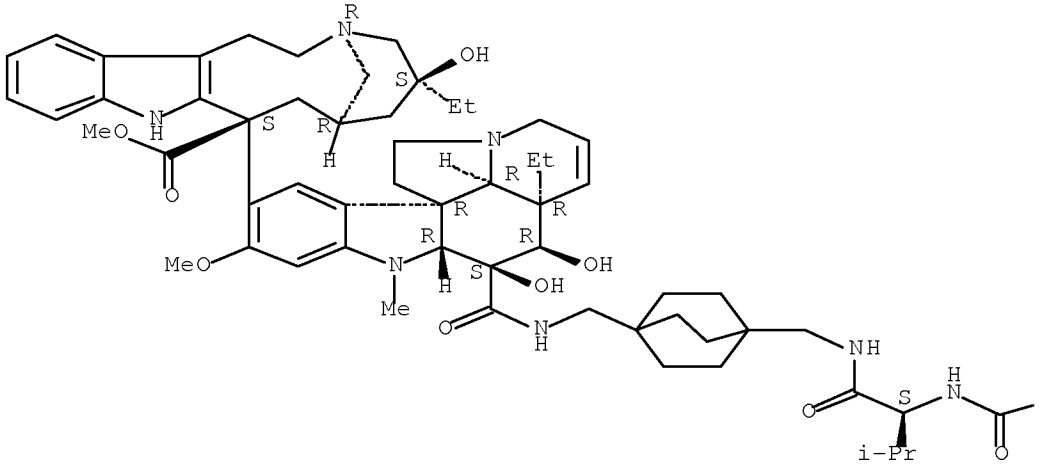
PAGE 2-B



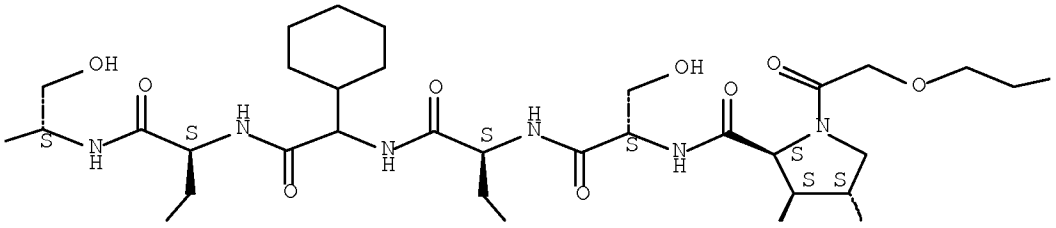
RN 219996-27-7 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (3S,4S)-3,4-dihydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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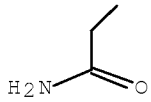
PAGE 2-B



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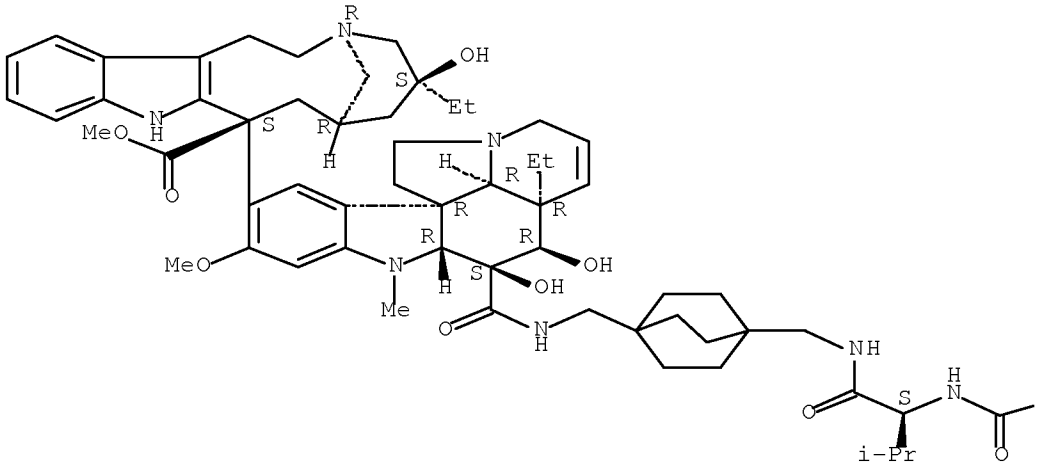
Absolute stereochemistry.

PAGE 1-A



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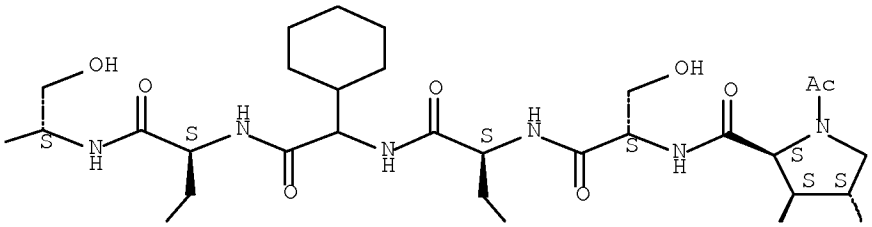

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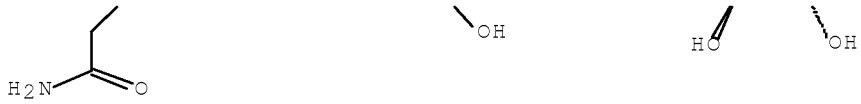

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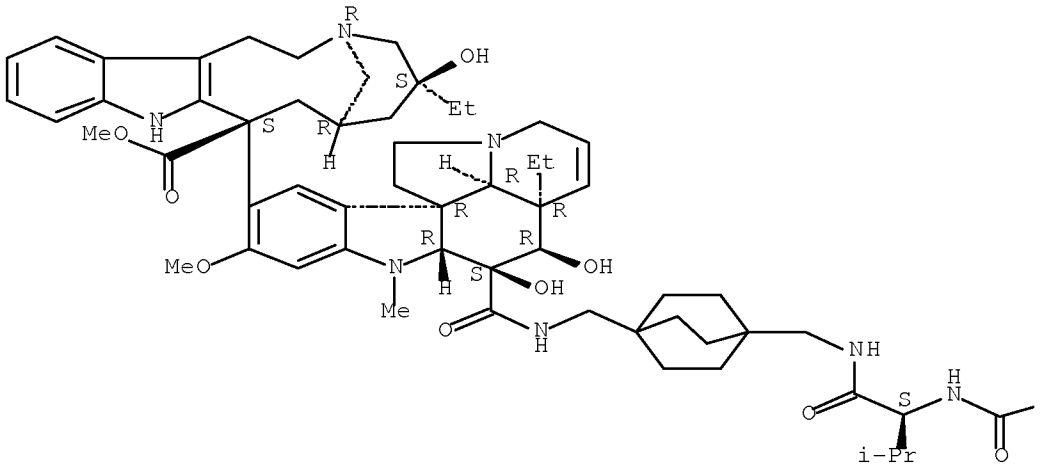
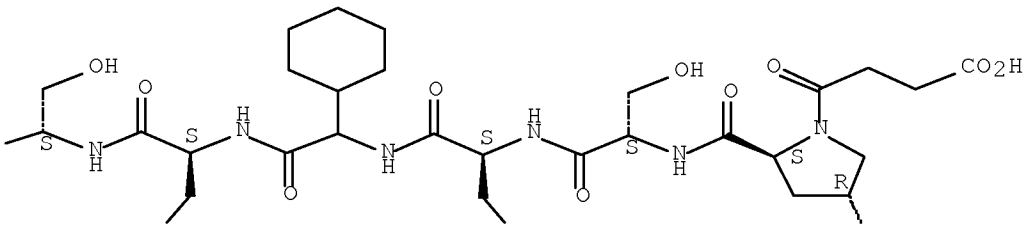
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-1-(3-carboxy-1-oxopropyl)-4-hydroxy-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

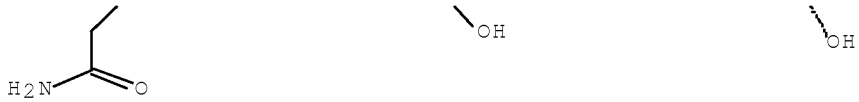
PAGE 1-A



PAGE 1-B



PAGE 2-B



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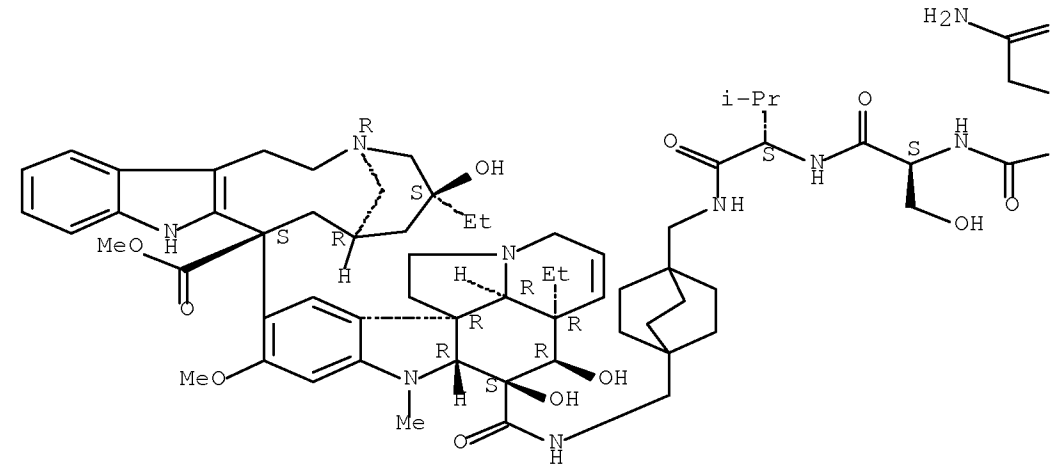
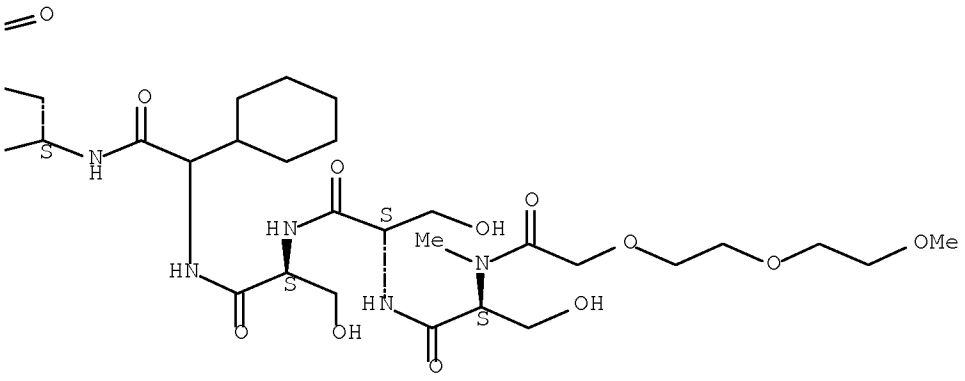
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-[[2-(2-methoxyethoxy)ethoxy]acetyl]-N-methyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



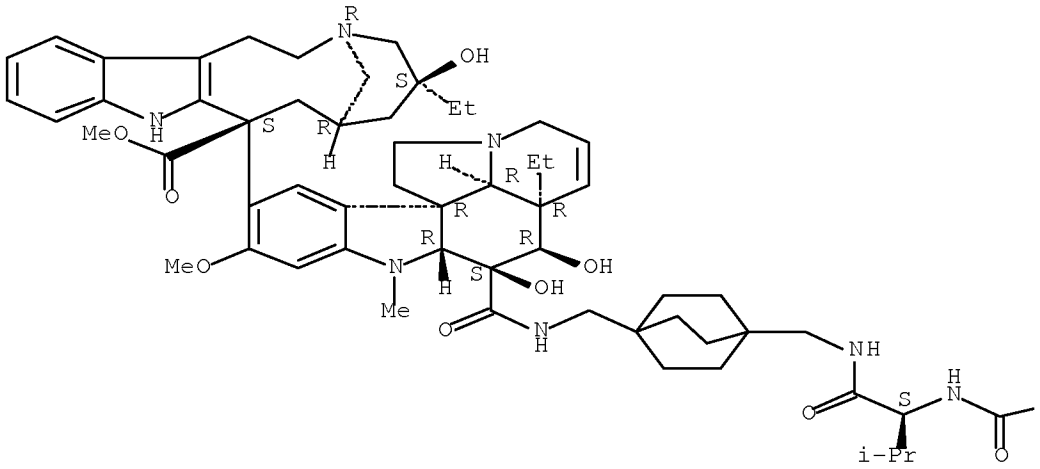
PAGE 1-B



RN 219996-31-3 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-methyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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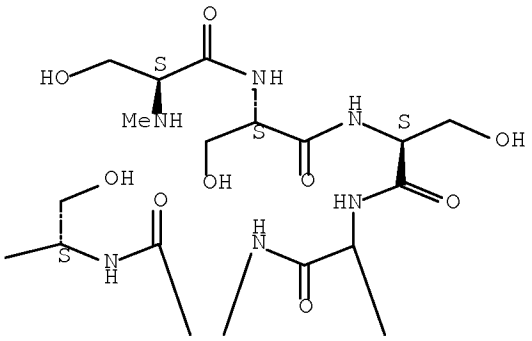


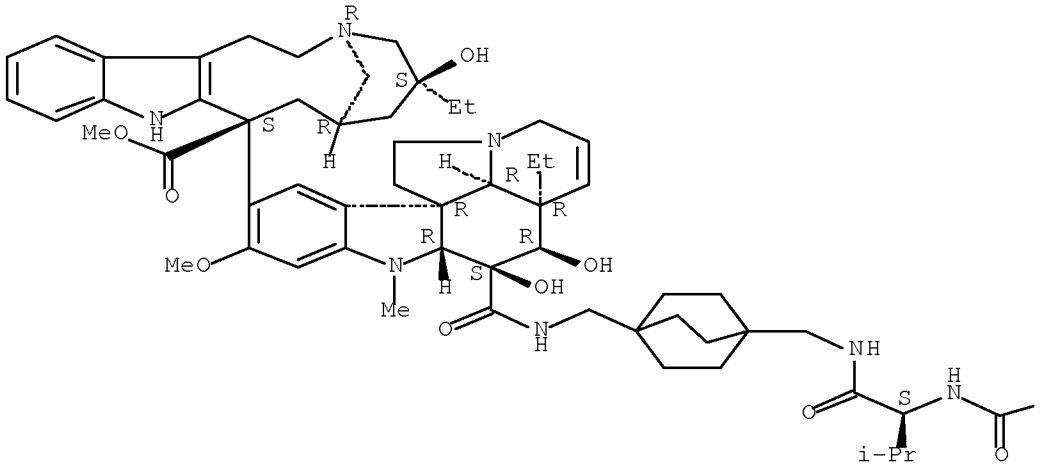
PAGE 2-B

RN 219996-32-4 HCAPLUS

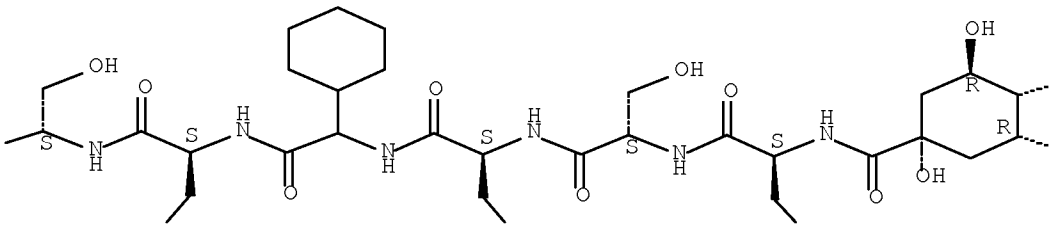
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 8-amide with (1α,3R,4α,5R)-1,3,4,5-tetrahydroxycyclohexanecarbonyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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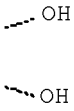
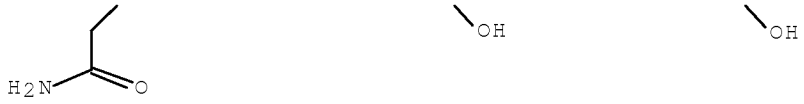


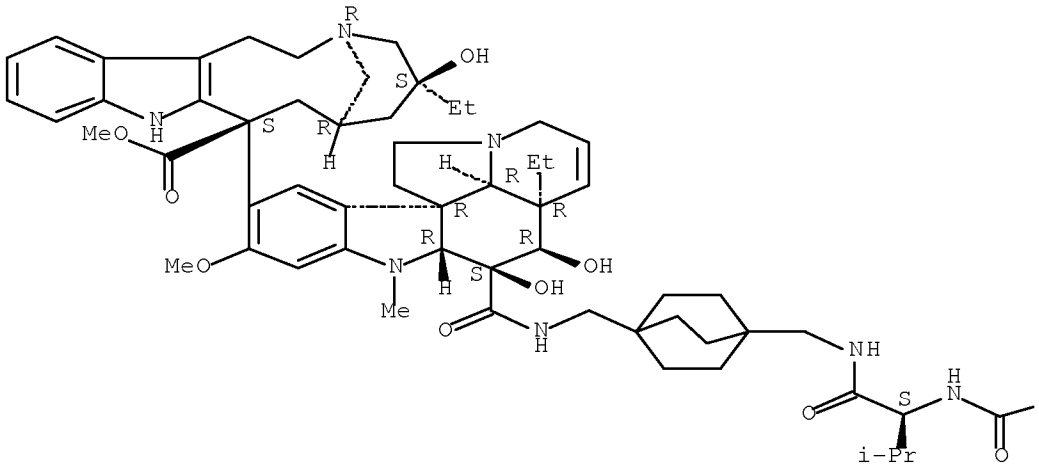
PAGE 2-B



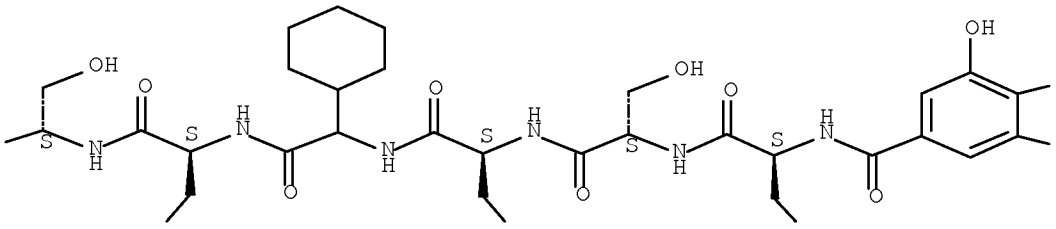
RN 219996-33-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-(3,4,5-trihydroxybenzoyl)-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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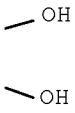
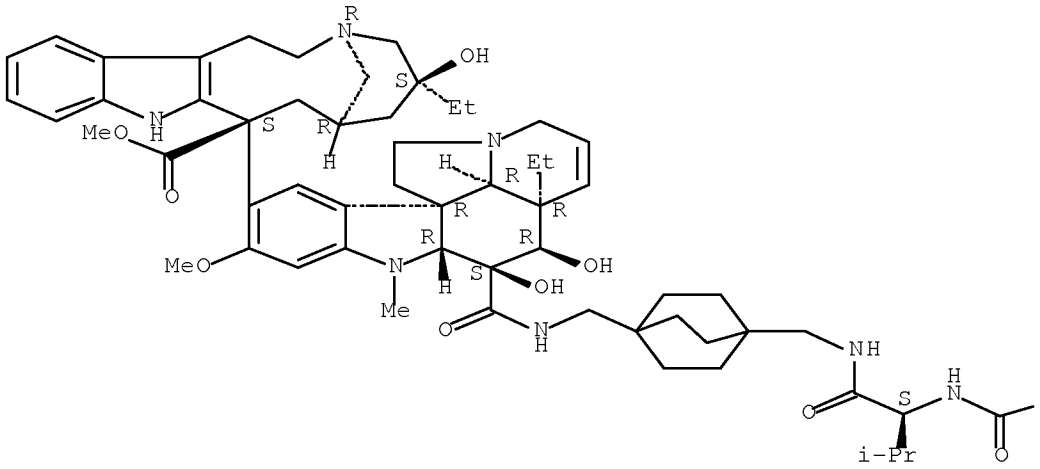


PAGE 2-B

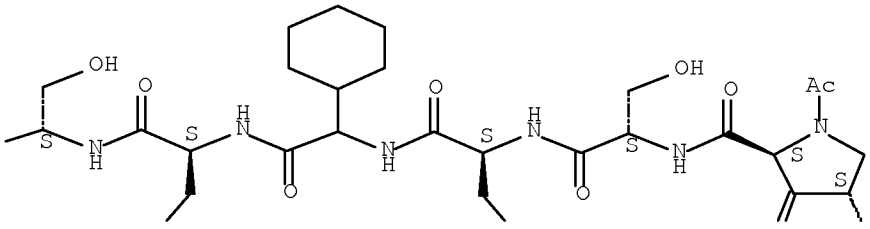
RN 219996-34-6 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4S)-1-acetyl-4-hydroxy-3-oxo-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

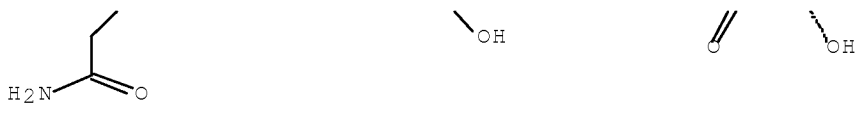
PAGE 1-A



PAGE 1-B



PAGE 2-B



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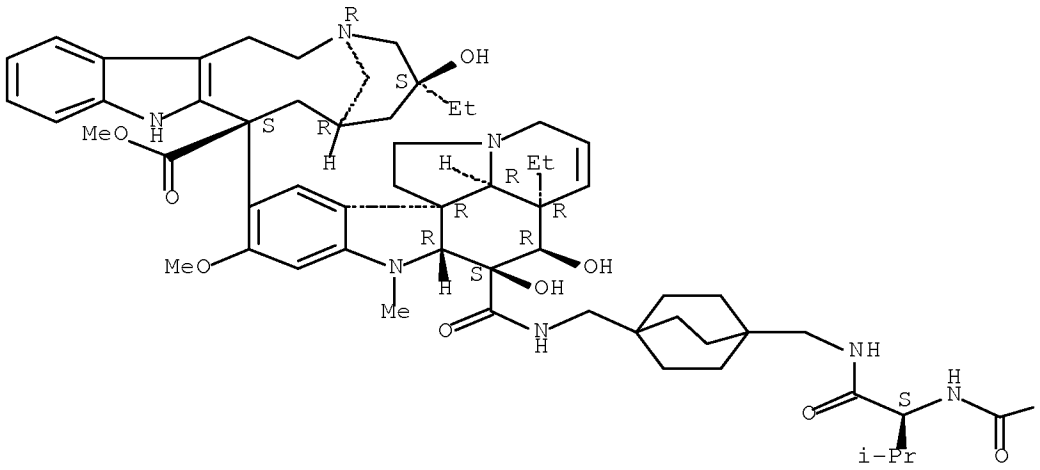
(4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-alanyl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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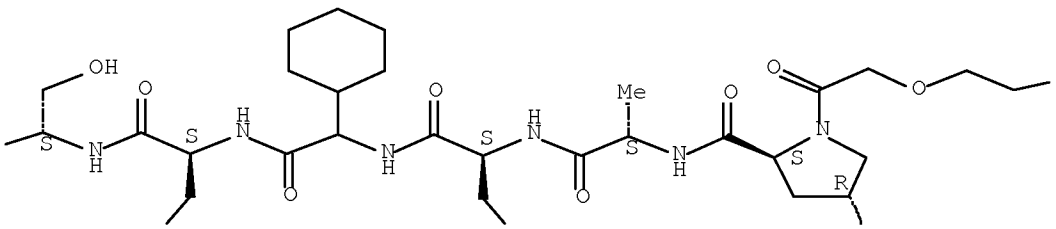
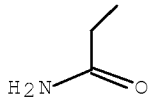


PAGE 1-C

PAGE 2-B



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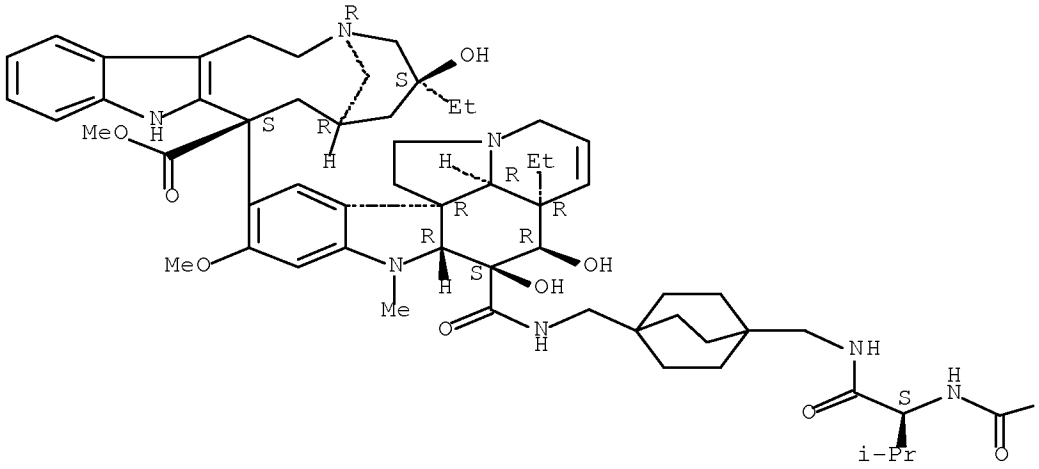
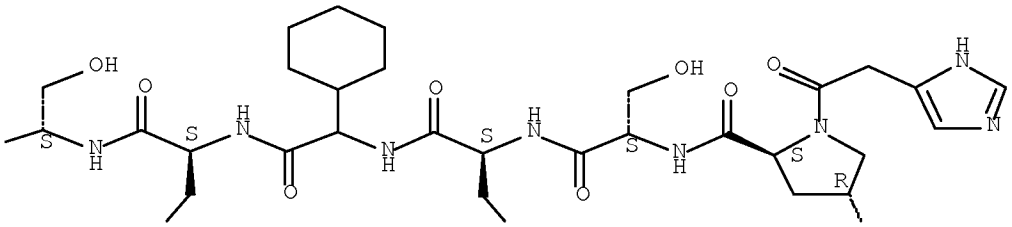
Absolute stereochemistry.

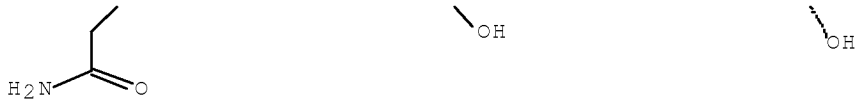
PAGE 1-A



PAGE 1-B



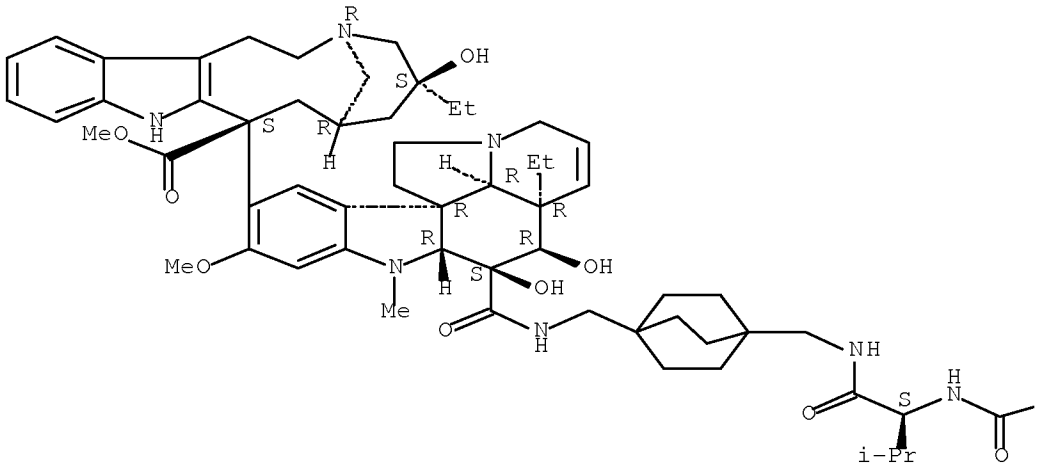
PAGE 2-B



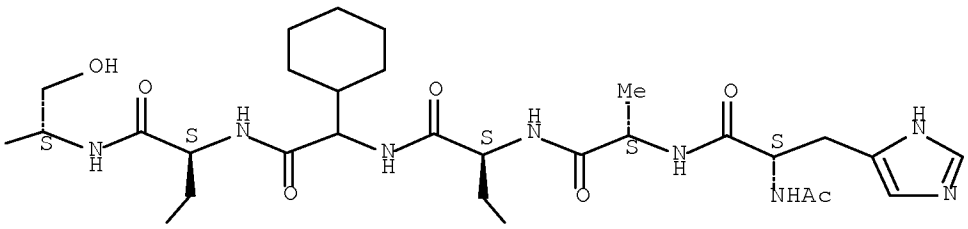
RN 219996-37-9 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-histidyl-L-alanyl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

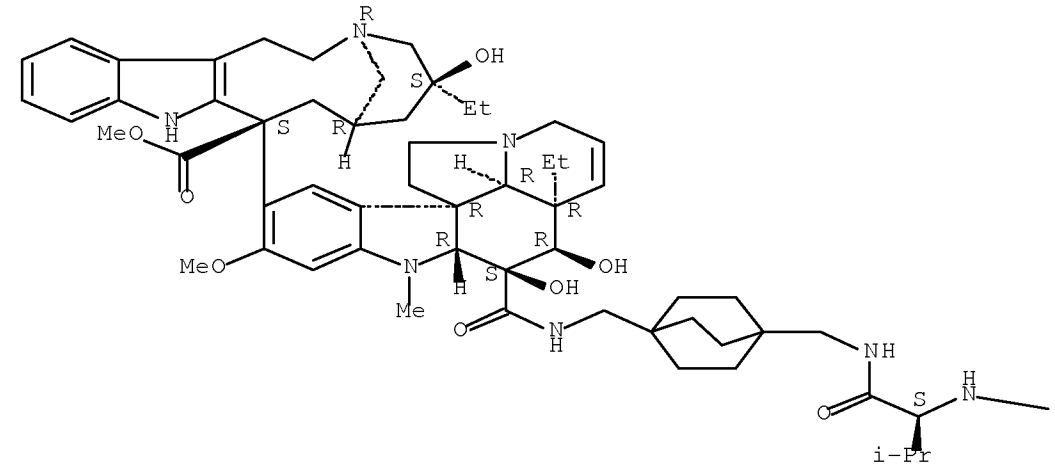


PAGE 2-B

RN 219996-38-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (2S)-2-[[[2-(2-methoxyethoxy)ethoxy]acetyl]amino]-4-sulfobutanoyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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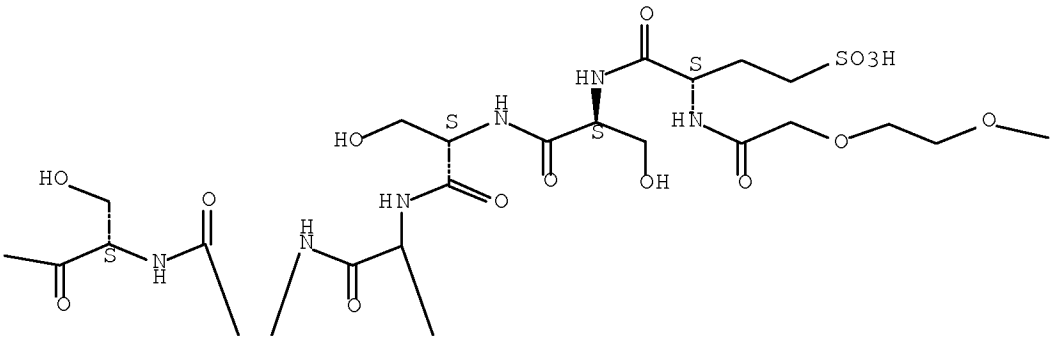
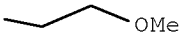


PAGE 1-C

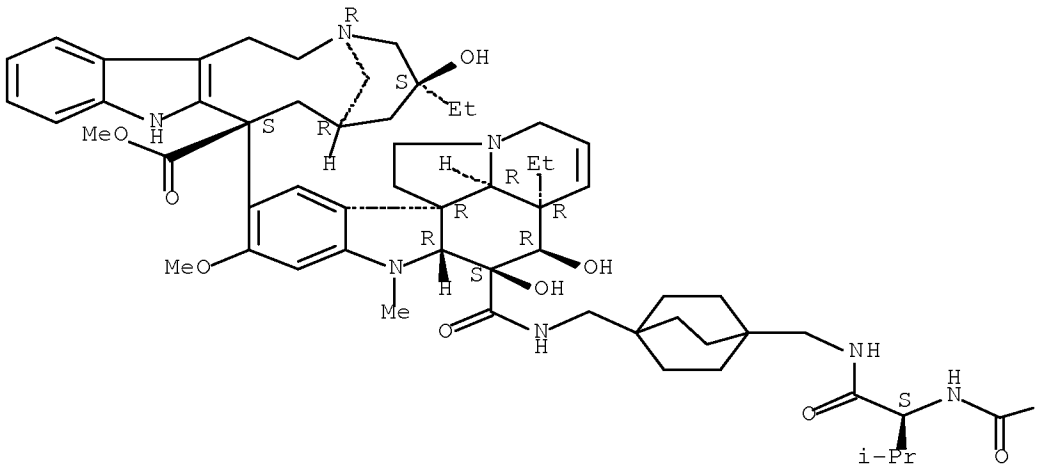


PAGE 2-B

RN 219996-39-1 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 8-amide with α-L-xylo-2-hexulofuranosonoyl-(4R)-4-hydroxy-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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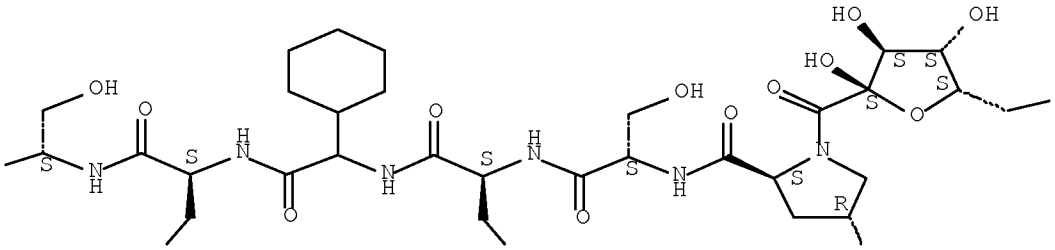
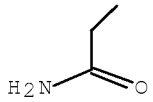


PAGE 1-C

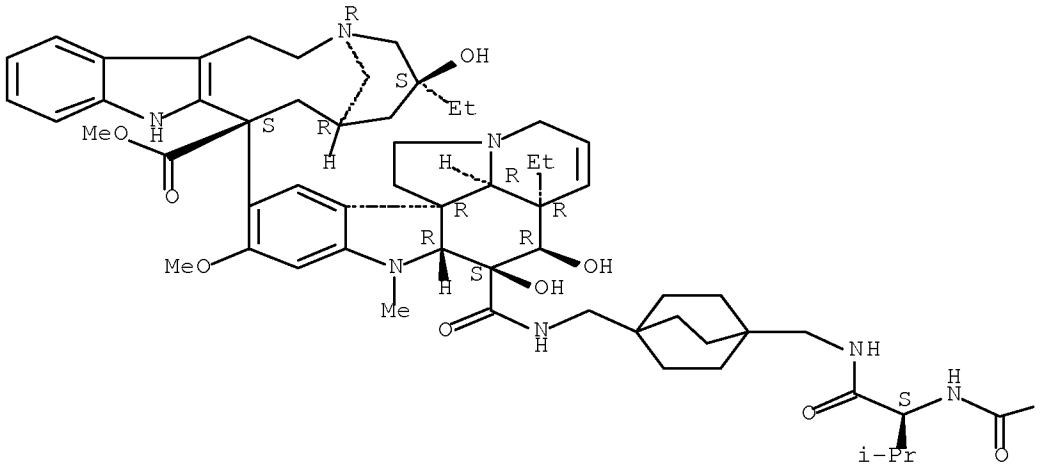
PAGE 2-B



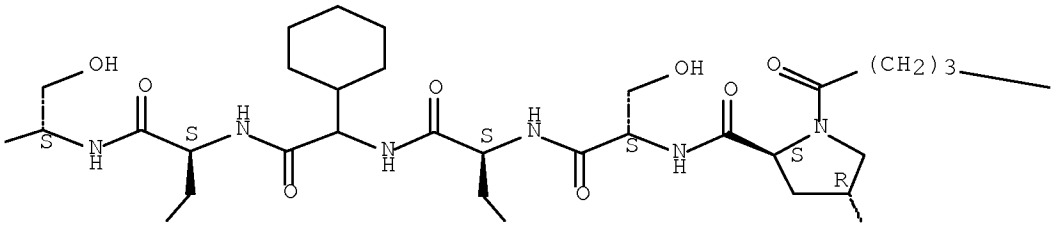
RN 219996-41-5 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-(1-oxo-4-phosphonobutyl)-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

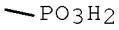
PAGE 1-A



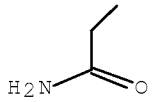
PAGE 1-B



PAGE 1-C



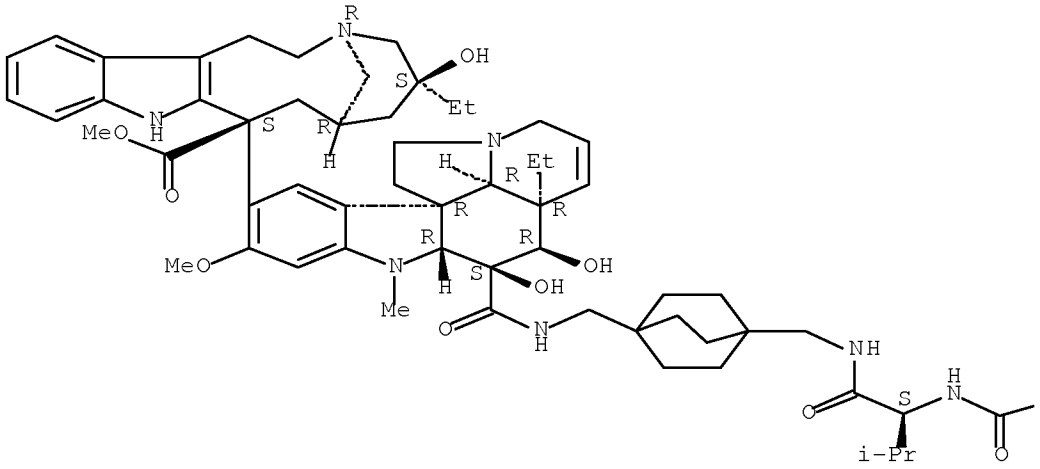
PAGE 2-B



RN 219996-42-6 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[(2S,3S)-1-methyl-5-oxo-2-(3-pyridinyl)-3-pyrrolidinyl]carbonyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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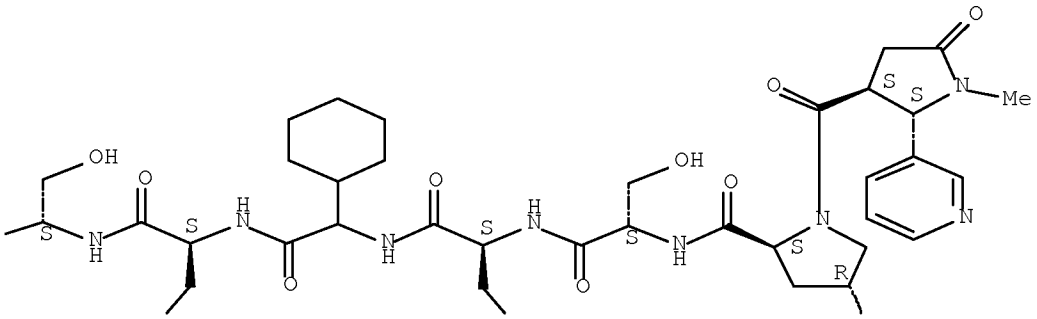
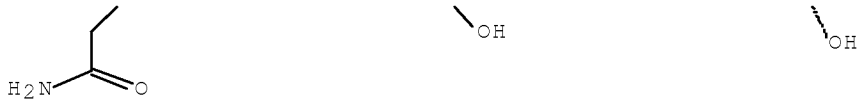


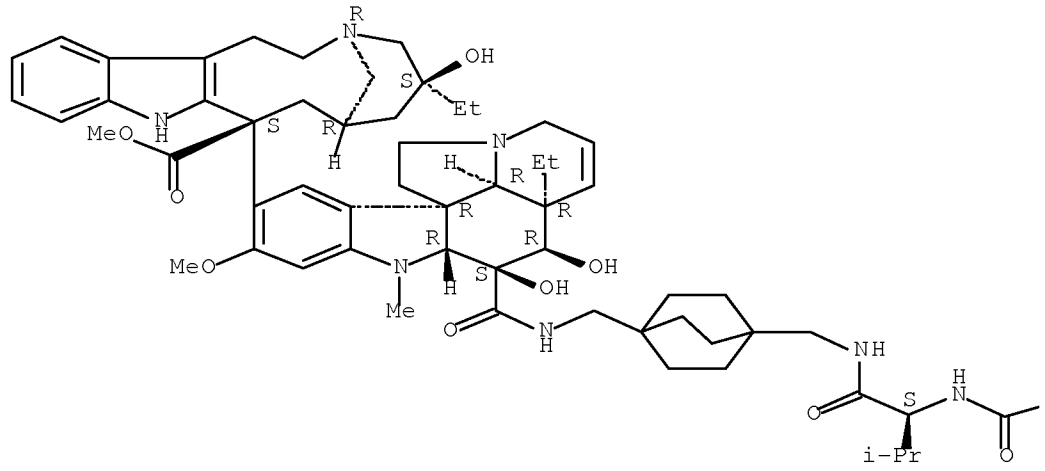
PAGE 2-B



RN 219996-43-7 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-(1-oxo-3-phosphonopropyl)-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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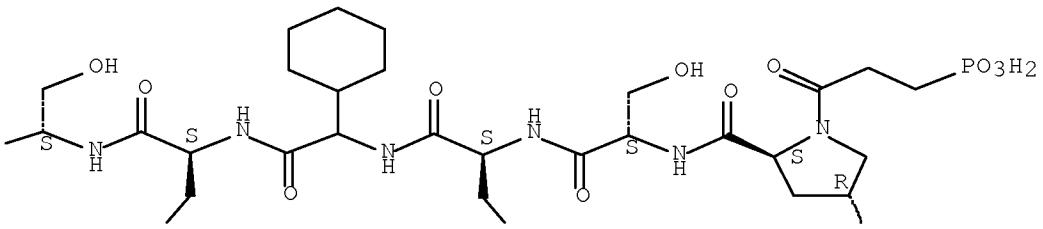
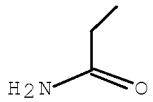


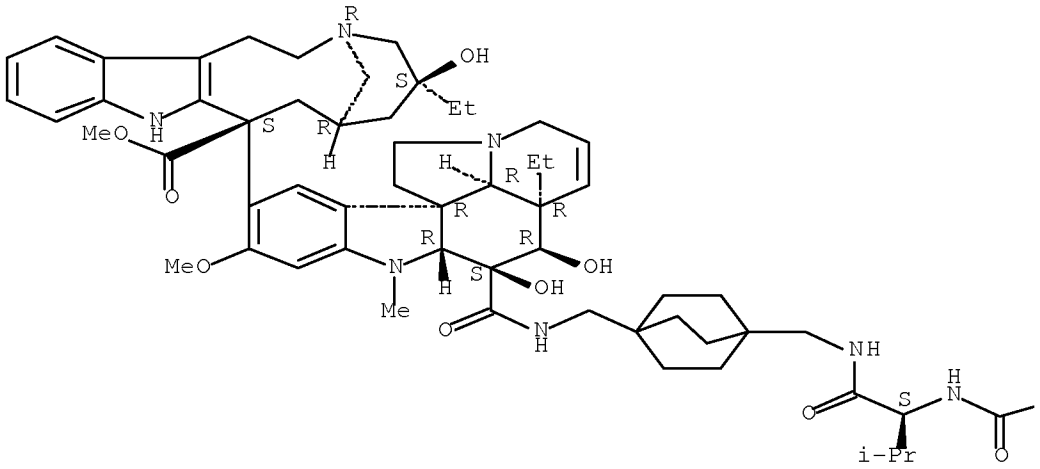
PAGE 2-B



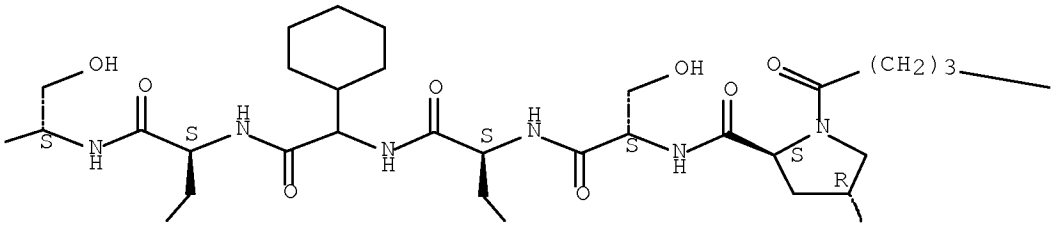
RN 219996-44-8 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-1-(4-carboxy-1-oxobutyl)-4-hydroxy-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

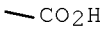
PAGE 1-A



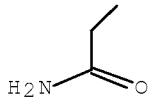
PAGE 1-B



PAGE 1-C



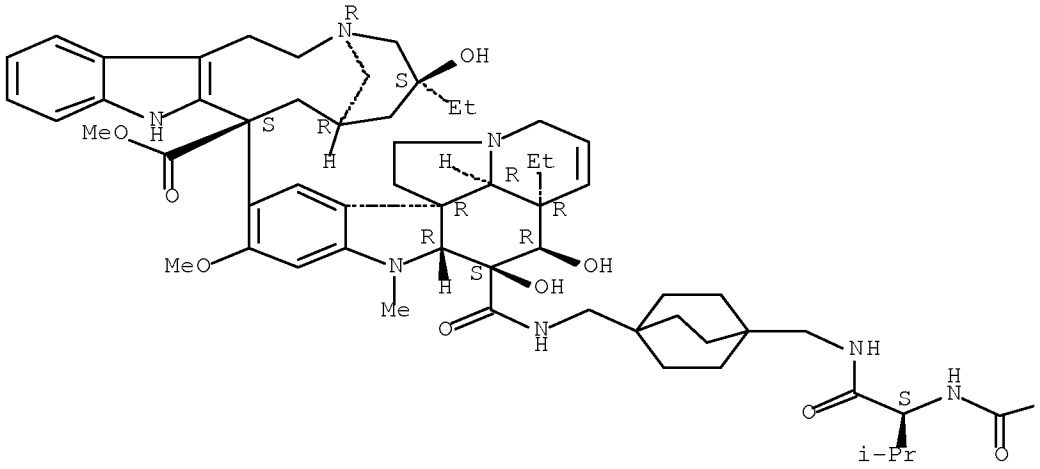
PAGE 2-B



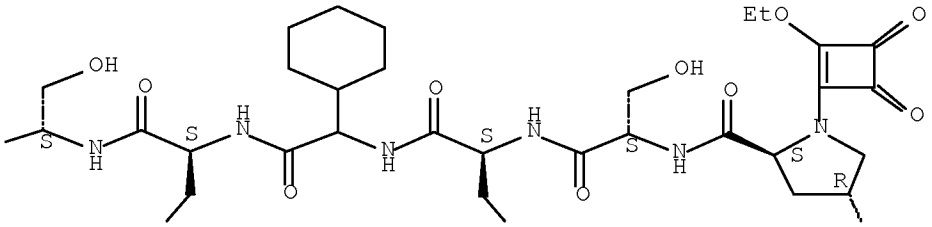
RN 219996-45-9 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-1-(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)-4-hydroxy-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

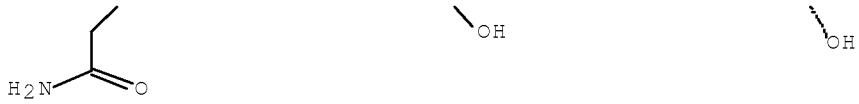
PAGE 1-A



PAGE 1-B



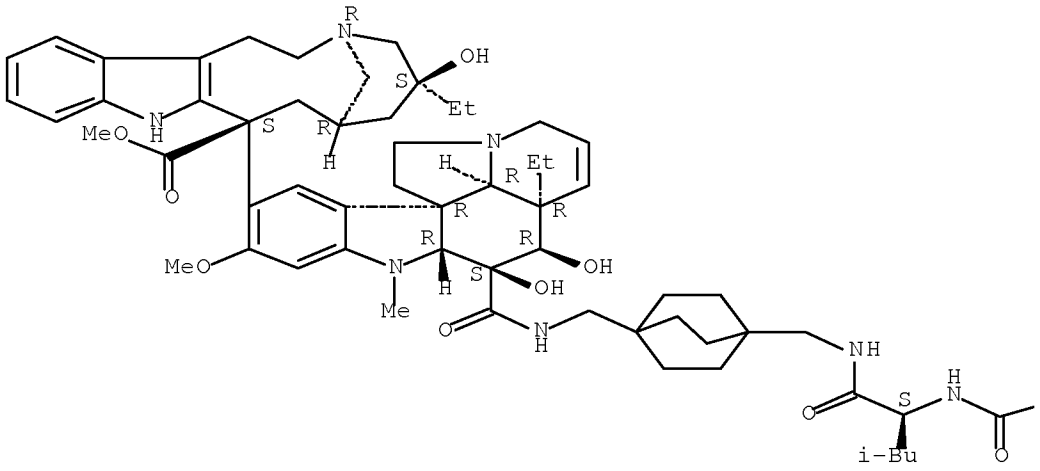
PAGE 2-B



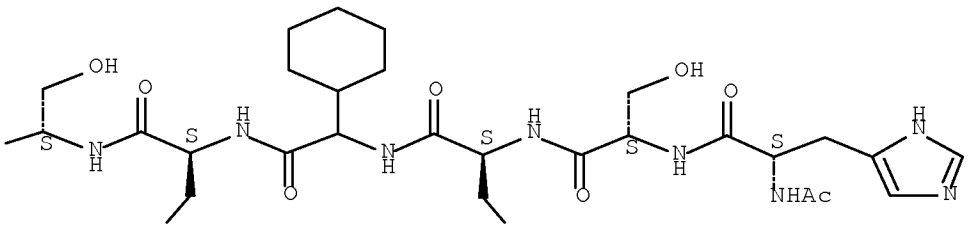
RN 219996-46-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-histidyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

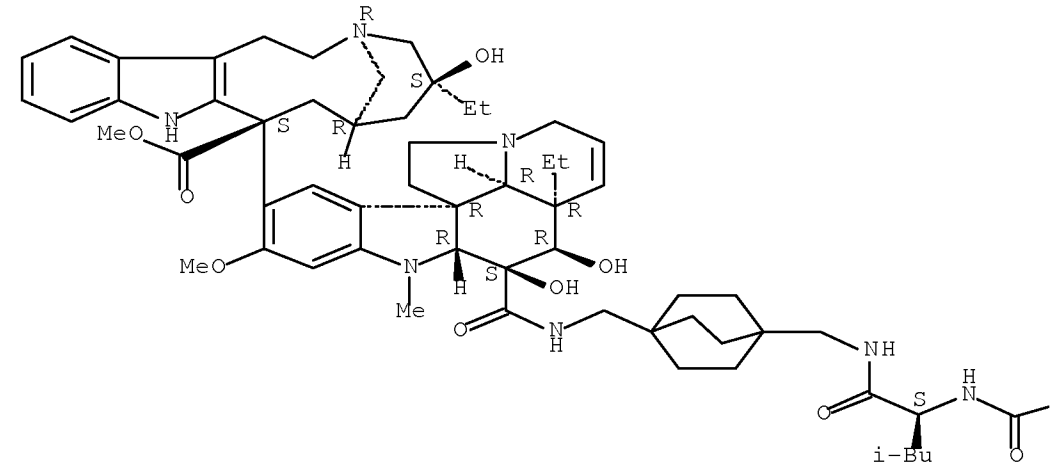


PAGE 2-B

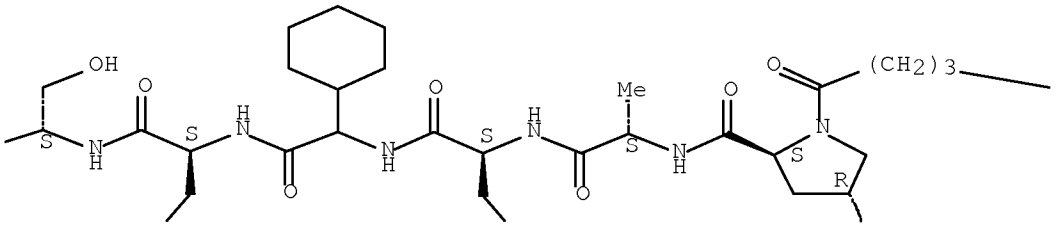
RN 219996-47-1 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-1-(4-carboxy-1-oxobutyl)-4-hydroxy-L-prolyl-L-alanyl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-leucinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

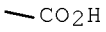
PAGE 1-A



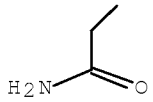
PAGE 1-B



PAGE 1-C



PAGE 2-B



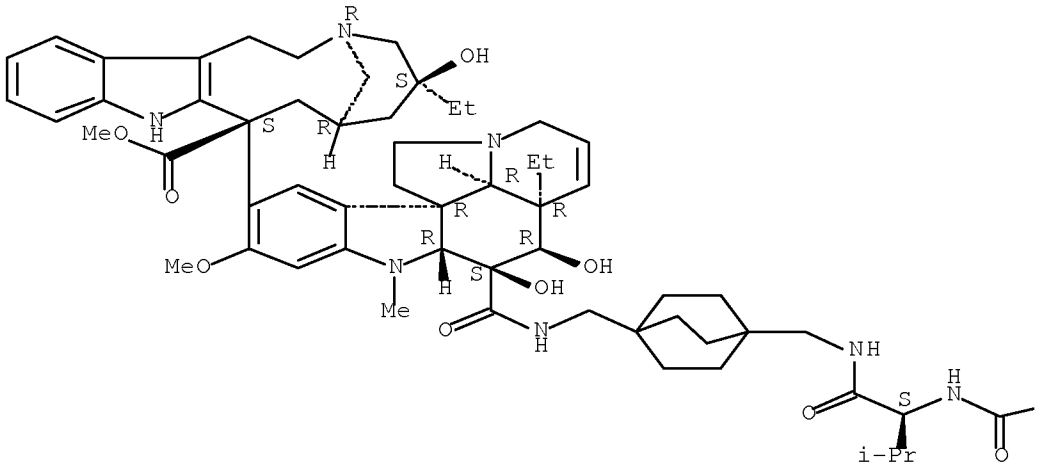
IT 219996-17-5P 219996-19-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

RN 219996-17-5 HCAPLUS

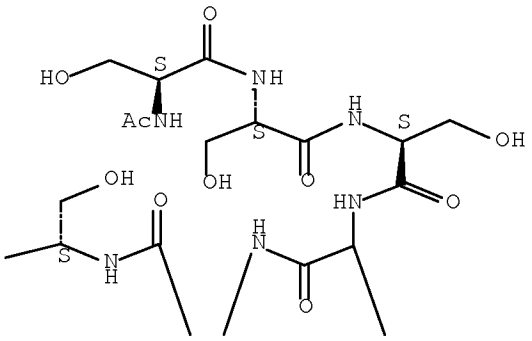
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



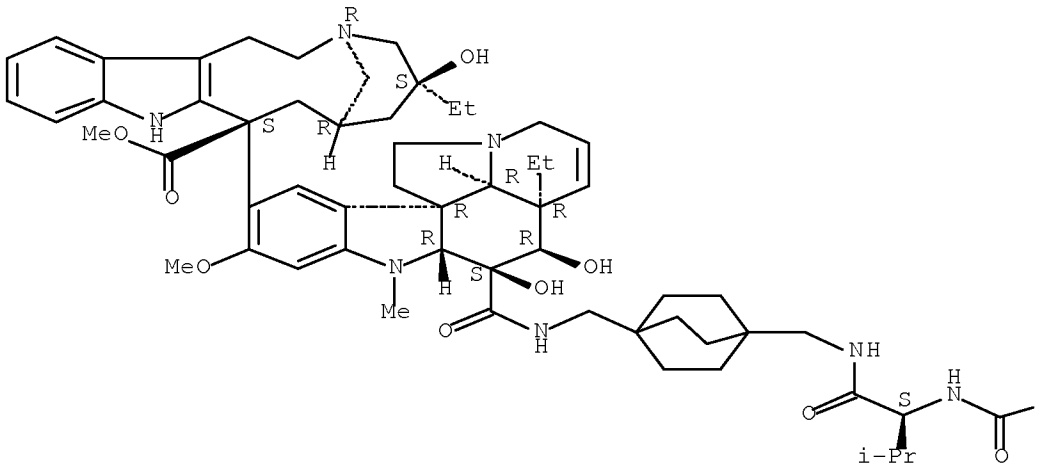
PAGE 2-B

RN 219996-19-7 HCAPLUS

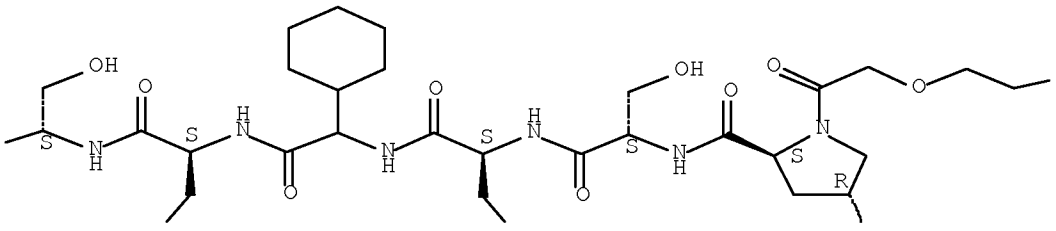
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

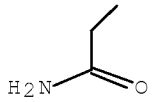


PAGE 1-B



PAGE 1-C

PAGE 2-B



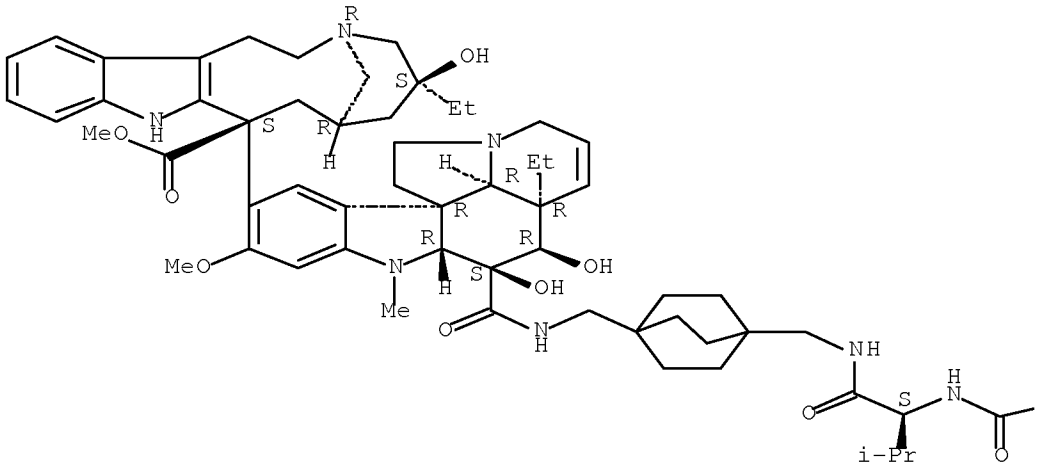
IT 219996-54-0P 219996-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
RN 219996-54-0 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with N-acetyl-L-seryl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

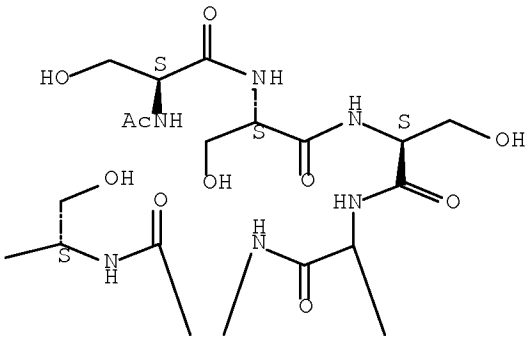
CRN 219996-17-5
CMF C85 H124 N14 O20

Absolute stereochemistry.

PAGE 1-A



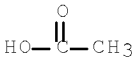
PAGE 1-B



PAGE 2-B

CM 2

CRN 64-19-7
CMF C2 H4 O2



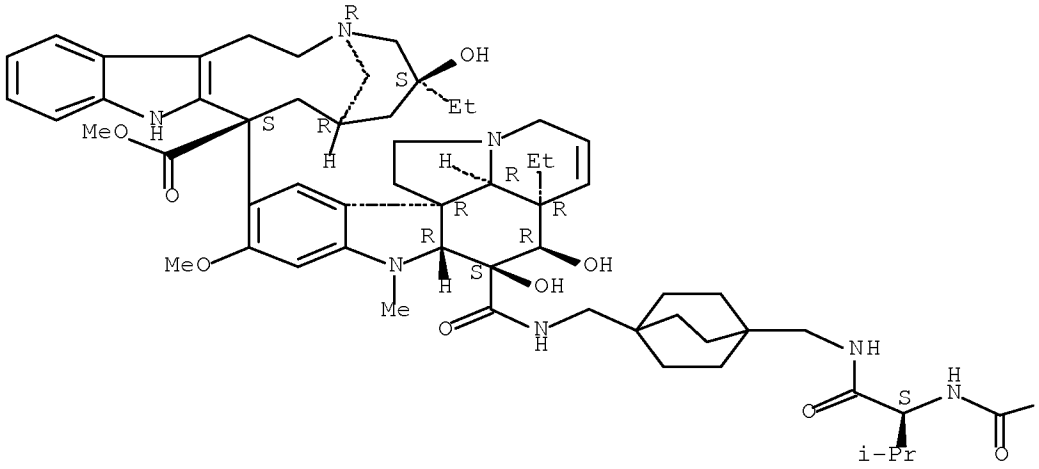
RN 219996-57-3 HCAPLUS
CN Vincaleukoblastin-23-oic acid, O4-deacetyl-, 7-amide with (4R)-4-hydroxy-1-[[2-(2-methoxyethoxy)ethoxy]acetyl]-L-prolyl-L-seryl-L-seryl-2-cyclohexylglycyl-L-glutaminyl-L-seryl-N-[[4-(aminomethyl)bicyclo[2.2.2]oct-1-yl]methyl]-L-valinamide, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

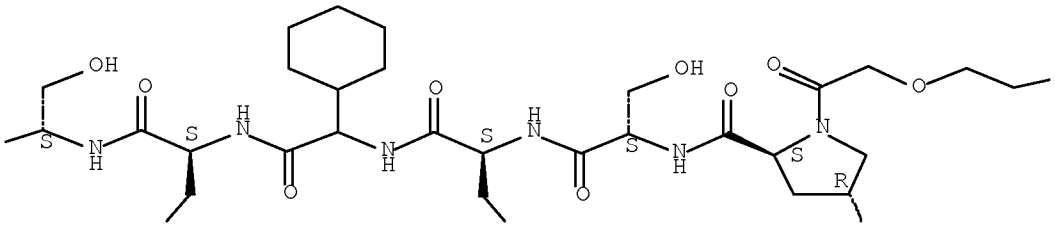
CRN 219996-19-7
CMF C92 H136 N14 O23

Absolute stereochemistry.

PAGE 1-A

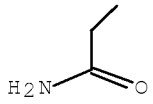


PAGE 1-B



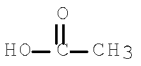
PAGE 1-C

PAGE 2-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



IC ICM A61K038-03
ICS A61K038-07; A61K038-08; C07K005-00; C07K007-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
IT Prostate gland
(benign hyperplasia; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Prostate gland
(neoplasm, inhibitors; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Peptides, reactions
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(oligopeptides, Vinca alkaloid conjugates; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Drug delivery systems
(prodrugs; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Antitumor agents
(prostate gland; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Prostate-specific antigen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(proteolytic cleavage by; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Drug delivery systems
(targeted; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vinca; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT 219996-18-6P 219996-20-0P 219996-21-1P 219996-22-2P
219996-24-4P 219996-25-5P 219996-26-6P
219996-27-7P 219996-28-8P 219996-29-9P
219996-30-2P 219996-31-3P 219996-32-4P
219996-33-5P 219996-34-6P 219996-35-7P
219996-36-8P 219996-37-9P 219996-38-0P
219996-39-1P 219996-41-5P 219996-42-6P
219996-43-7P 219996-44-8P 219996-45-9P
219996-46-0P 219996-47-1P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)
IT 219996-17-5P 219996-19-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 865-21-4, Vinblastine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 865-21-4DP, Vinblastine, oligopeptide conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 174639-59-9 174639-73-7 174640-61-0 174640-62-1 174640-63-2
174640-72-3 174640-73-4 189510-08-5 189510-10-9 205183-77-3
205183-79-5 205183-95-5 205184-26-5 219995-91-2 219995-92-3
219995-93-4 219995-94-5 219995-95-6 219995-96-7 219995-97-8
219995-98-9 219995-99-0 219996-00-6 219996-01-7 219996-02-8
219996-03-9 219996-04-0 219996-05-1 219996-07-3 219996-08-4
219996-09-5 219996-10-8 219996-11-9 219996-12-0 219996-13-1
219996-14-2 219996-15-3 219996-16-4
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 13734-41-3D, PAM resin conjugates
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 219996-53-9DP, PAM resin conjugates
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 57-22-7D, Vincristine, oligopeptide conjugates 3352-69-0D, 4-Desacetylvinblastine, oligopeptide conjugates 15228-71-4D, Leurosidine, oligopeptide conjugates 53643-48-4, Vindesine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 55383-37-4P 219996-48-2P 219996-49-3P 219996-50-6P 219996-51-7P
219996-52-8P 219996-54-0P 219996-55-1DP, PAM resin conjugates
219996-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of; oligopeptide-Vinca alkaloid conjugates useful in the treatment of prostate cancer)

IT 64-19-7, Acetic acid, reactions 66-40-0, Tea 110-46-3, Isoamyl nitrite 143-67-9, Vinblastine sulfate 302-01-2, Hydrazine, reactions 530-62-1 13726-85-7 16024-58-1 23680-31-1 24238-86-6 25952-53-8, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride 29684-56-8 35264-05-2 39968-33-7, 1-Hydroxy-7-azabenzotriazole 54631-81-1 58632-95-4, Boc-on
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; oligopeptide-Vinca alkaloid conjugates useful in the

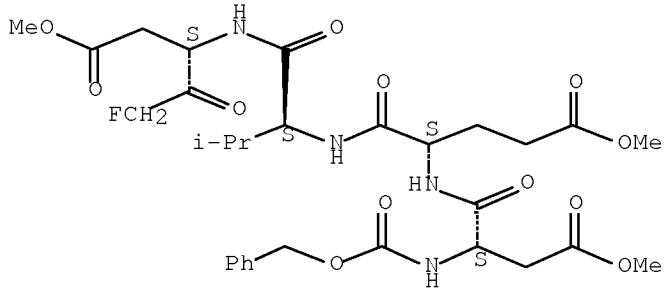
treatment of prostate cancer)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 49 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:800664 HCAPLUS Full-text
DOCUMENT NUMBER: 130:150428
TITLE: Hypericin-induced photosensitization of HeLa cells leads to apoptosis or necrosis involvement of cytochrome c and procaspase-3 activation in the mechanism of apoptosis
AUTHOR(S): Vantieghem, Annelies; Assefa, Zerihun; Vandenabeele, Peter; Declercq, Wim; Courtois, Stephane; Vandenheede, Jackie R.; Merlevede, Wilfried; de Witte, Peter; Agostinis, Patrizia
CORPORATE SOURCE: Division of Biochemistryv, Faculty of Medicine, KU Leuven, Leunven, B-3000, Belg.
SOURCE: FEBS Letters (1998), 440(1,2), 19-24
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Here we report that photoactivated hypericin can induce either apoptosis or necrosis in HeLa cells. Under apoptotic conditions the cleavage of poly(ADP-ribose) polymerase (PARP) into the 85-kDa product is blocked by the caspase inhibitors benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone (z-VAD-fmk) and benzyloxycarbonyl-Asp-Glu-Val-Asp-fluoromethylketone (z-DEVD-fmk). Both inhibitors protect cells from apoptosis but cannot prevent hypericin-induced necrosis. Conversely, HeLa cells overexpressing the viral cytokine response modifier A (CrmA), which inhibits caspase-1 and -8, still undergo hypericin-induced apoptosis and necrosis. Evidence is provided for the release of mitochondrial cytochrome c in the cytosol and for procaspase-3 activation in the hypericin-induced cell killing.

IT 210344-95-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypericin-induced photosensitization of HeLa cells leads to apoptosis or necrosis involvement of cytochrome c and procaspase-3 activation in the mechanism of apoptosis)
RN 210344-95-9 HCAPLUS
CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

Absolute stereochemistry.



CC 8-9 (Radiation Biochemistry)
ST hypericin photosensitization tumor apoptosis necrosis; cytochrome procaspase tumor photosensitization hypericin
IT Apoptosis
Necrosis
Neoplasm
Photodynamic therapy
Photosensitizers (pharmaceutical)
(hypericin-induced photosensitization of HeLa cells leads to apoptosis or necrosis involvement of cytochrome c and procaspase-3 activation in the mechanism of apoptosis)
IT 187389-52-2 210344-95-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypericin-induced photosensitization of HeLa cells leads to apoptosis or necrosis involvement of cytochrome c and procaspase-3 activation in the mechanism of apoptosis)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

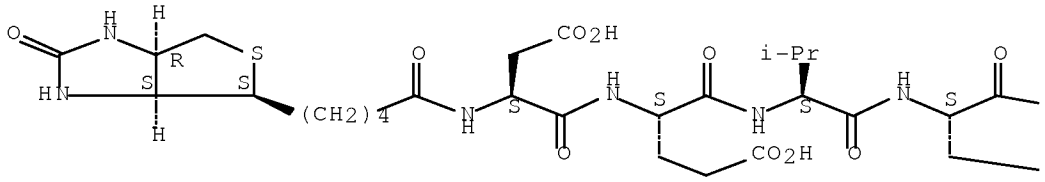
L76 ANSWER 50 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:568911 HCAPLUS Full-text
DOCUMENT NUMBER: 129:184238
ORIGINAL REFERENCE NO.: 129:37273a,37276a
TITLE: Screening for thymocyte caspase activity modulators
INVENTOR(S): Reinherz, Ellis; Clayton, Linda; Ocain, Timothy D.; Patch, Raymond J.
PATENT ASSIGNEE(S): Dana Farber Cancer Institute, USA; Procept, Inc.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9836057	A1	19980820	WO 1998-US3524		19980217
W: CA, JP					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 7247438	B1	20070724	US 1997-948124		19971009
PRIORITY APPLN. INFO.:			US 1997-802474	A	19970218
			US 1997-948124	A	19971009

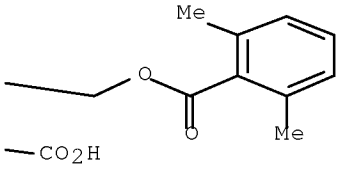
AB Work described herein shows that T cell receptor triggering by peptide/MHC ligands activates a caspase in thymocytes, including CD4+CD8+ double pos. thymocytes, resulting in their death. Methods of inhibiting apoptosis in thymocytes are described, as well as assays for identifying an agent which alters the activity of the caspase are described.
IT 191666-52-1P 211918-99-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(screening for thymocyte caspase activity modulators)
RN 191666-52-1 HCAPLUS
CN L-Valinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-L-α-aspartyl-L-α-glutamyl-N-[(1S)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



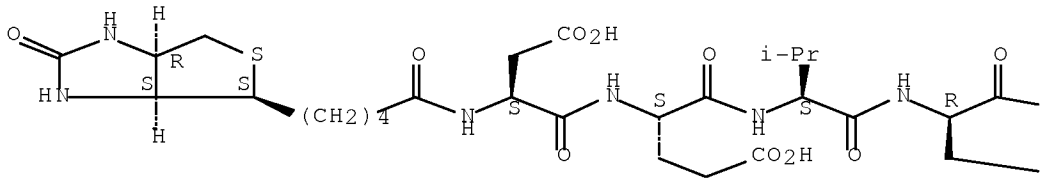
PAGE 1-B



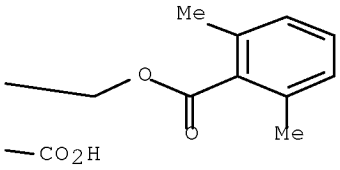
RN 211918-99-9 HCAPLUS
CN L-Valinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-L-α-aspartyl-L-α-glutamyl-N-[(1R)-1-(carboxymethyl)-3-[(2,6-dimethylbenzoyl)oxy]-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IC ICM C12N009-50
CC 1-1 (Pharmacology)

Section cross-reference(s): 7

IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tumor-associated; screening for thymocyte caspase activity modulators)

IT 187389-52-2P 191666-52-1P 211918-95-5P 211918-96-6P
211918-97-7P 211918-98-8P 211918-99-9P 211919-00-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(screening for thymocyte caspase activity modulators)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 51 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:351096 HCAPLUS Full-text
DOCUMENT NUMBER: 126:317669
ORIGINAL REFERENCE NO.: 126:61629a,61632a
TITLE: Preparation of thio-substituted peptides as inhibitors for collagenase, stromelysin and tumor necrosis factor liberation
INVENTOR(S): Baxter, Andrew Douglas; Montana, John Gary; Owen, David Alan
PATENT ASSIGNEE(S): Chiroscience Limited, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9712902	A1	19970410	WO 1996-GB2438	19961004
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
CA 2229434	A1	19970410	CA 1996-2229434	19961004
AU 9671398	A	19970428	AU 1996-71398	19961004
AU 710072	B2	19990916		
EP 859784	A1	19980826	EP 1996-932722	19961004
EP 859784	B1	20021218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1198747	A	19981111	CN 1996-197437	19961004
CN 1145637	C	20040414		
JP 11512733	T	19991102	JP 1996-514078	19961004
US 5981490	A	19991109	US 1996-725781	19961004
BR 9610922	A	19991221	BR 1996-10922	19961004
HU 2000003760	A2	20010428	HU 2000-3760	19961004
HU 2000003760	A3	20010528		
IL 123430	A	20010430	IL 1996-123430	19961004
CZ 289711	B6	20020313	CZ 1998-1017	19961004
AT 229972	T	20030115	AT 1996-932722	19961004
PL 185312	B1	20030430	PL 1996-325824	19961004
ES 2186803	T3	20030516	ES 1996-932722	19961004
ZA 9608436	A	19971121	ZA 1996-8436	19961007

NO 9801520	A	19980403	NO 1998-1520		19980403
PRIORITY APPLN. INFO.:			GB 1995-20354	A	19951005
			GB 1996-7126	A	19960404
			WO 1996-GB2438	W	19961004

OTHER SOURCE(S): MARPAT 126:317669

AB Alkylmercaptopeptides R7SCH(R8)CON(R15)CH(R1)CON(R2)Y(R6)X [X = heteroaryl, (substituted) carboxamide; Y = C1-6 alkyl, C2-6 alkenyl, bond; R6 = C3-6 cycloalkyl, C3-6 cycloalkenyl, C1-6 alkyl, C1-6 alkoxyaryl, aryl, heteroaryl, C1-3 alkylaryl, (substituted) carboxy, (substituted) carboxamide, (substituted) sulfonamide, etc.; R2 = H, C1-6 alkyl; R15 = (substituted) amino, (substituted) ester, (substituted) carboxamide, etc.; R8 = H, C1-4 alkyl; R7 = H, acyl groups containing alkyl, alkylaryl, alkenyl, alkenylaryl, cycloalkyl, cycloalkyl, aryl, heteroaryl, etc.] and their salts, solvates and hydrates were prepared These compds. are useful inhibitors of matrix metalloproteinases and/or of tumor necrosis factor (TNF) release, which mediate certain degenerative diseases and cancers.

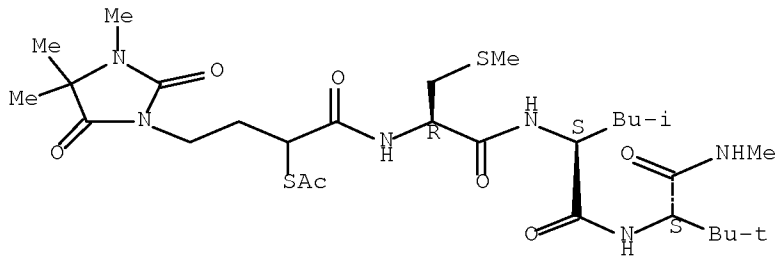
IT 189443-50-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)

RN 189443-50-3 HCAPLUS

CN L-Valinamide, N-[2-(acetylthio)-1-oxo-4-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)butyl]-S-methyl-L-cysteinyl-L-leucyl-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



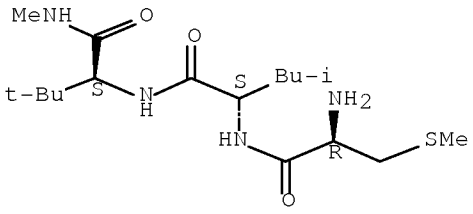
IT 189443-51-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)

RN 189443-51-4 HCAPLUS

CN L-Valinamide, S-methyl-L-cysteinyl-L-leucyl-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K005-03
ICS C07K005-033; A61K038-07
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
ST peptide alkylmercapto prepn matrix metalloproteinase inhibitor; tumor necrosis factor release inhibitor mercaptopeptide
IT Neoplasm
(metastasis, treatment; preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)
IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)
IT 189443-42-3P 189443-46-7P 189443-48-9P 189443-50-3P
189443-52-5P 189443-54-7P 189443-55-8P 189443-56-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)
IT 189443-44-5P 189443-47-8P 189443-49-0P 189443-51-4P
189443-53-6P 189443-57-0P 189443-58-1P 189443-59-2P 189443-60-5P
189443-61-6P 189443-62-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of mercaptopeptides as inhibitors of matrix metalloproteinases and TNF release)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 52 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:248955 HCAPLUS Full-text
DOCUMENT NUMBER: 124:333070
ORIGINAL REFERENCE NO.: 124:61537a,61540a
TITLE: Preparation of peptides as antitumor agents
INVENTOR(S): Haupt, Andreas; Janssen, Bernd; Ritter, Kurt; Klinge, Dagmar; Keilhauer, Gerhard; Romerdahl, Cynthia; Barlozzari, Teresa; Qian, Xiao Dong
PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: U.S., 36 pp., Cont.-in-part of U. S. Ser. No. 991,309, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5502032	A	19960326	US 1994-178529	19940105
CA 2151953	A1	19940623	CA 1993-2151953	19931204
HU 72067	A2	19960328	HU 1995-1754	19931204
CZ 286752	B6	20000614	CZ 1995-1575	19931204
ES 2151921	T3	20010116	ES 1994-902676	19931204
IL 107987	A	19991028	IL 1993-107987	19931210
TW 400335	B	20000801	TW 1993-82110574	19931214
ZA 9309389	A	19950615	ZA 1993-9389	19931215
CN 1095724	A	19941130	CN 1993-112646	19931216
CN 1057095	C	20001004		
HR 931504	B1	20010430	HR 1993-1504	19931216

PRIORITY APPLN. INFO.: US 1992-991309 B2 19921216

OTHER SOURCE(S): MARPAT 124:333070

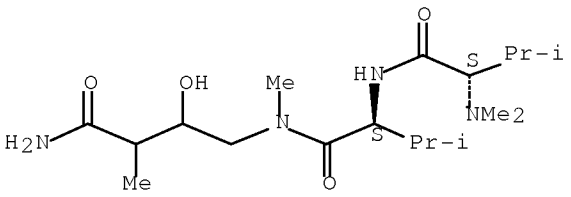
AB Novel peptides containing benzene, heterocyclic rings are prepared and have antitumor activity. Thus, a peptide was prepared from phenylalanine-HCl, BOC-NMeCH(CHMe2)CH(OMe)CH2CO2H, and N-tert-butyloxycarbonylvaline-N-carboxyanhydride. The peptides can be used for tumor treatment.

IT 176768-47-1P 176768-48-2P 176768-55-1P
176768-67-5P 176768-96-0P 176769-02-1P
176769-05-4P 176769-06-5P 176769-13-4P
176769-36-1P 176769-37-2P 176769-38-3P
176769-39-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as antitumor agents)

RN 176768-47-1 HCAPLUS

CN L-Valinamide, N,N-dimethyl-L-valyl-N-(4-amino-2-hydroxy-3-methyl-4-oxobutyl)-N-methyl- (9CI) (CA INDEX NAME)

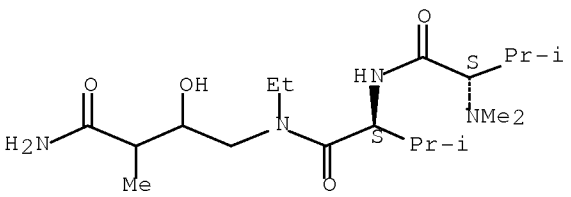
Absolute stereochemistry.



RN 176768-48-2 HCAPLUS

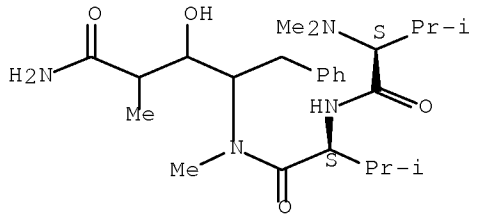
CN L-Valinamide, N,N-dimethyl-L-valyl-N-(4-amino-2-hydroxy-3-methyl-4-oxobutyl)-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



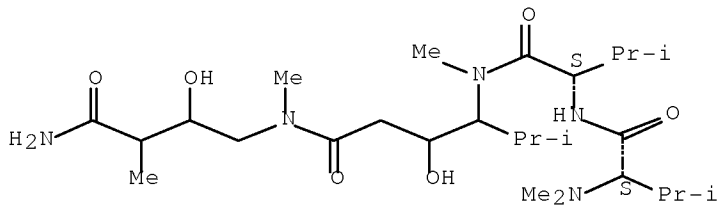
RN 176768-55-1 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[4-amino-2-hydroxy-3-methyl-4-oxo-1-(phenylmethyl)butyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



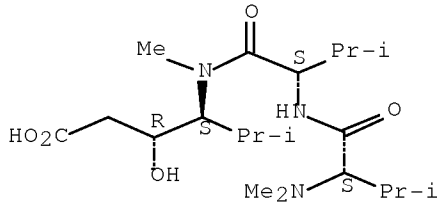
RN 176768-67-5 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[4-[(4-amino-2-hydroxy-3-methyl-4-oxobutyl)methylamino]-2-hydroxy-1-(1-methylethyl)-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 176768-96-0 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[3-carboxy-2-hydroxy-1-(1-methylethyl)propyl]-N-methyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

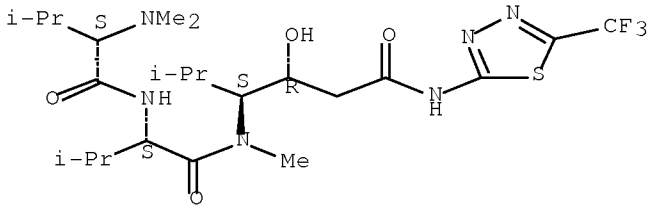
Absolute stereochemistry.



RN 176769-02-1 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[2-hydroxy-1-(1-methylethyl)-4-oxo-4-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino]butyl]-N-methyl-,

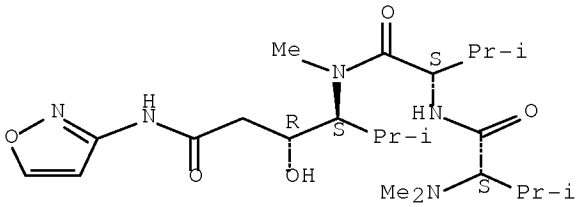
[R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



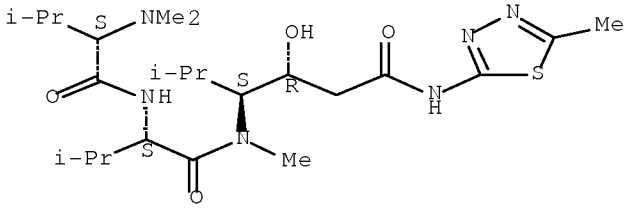
RN 176769-05-4 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[2-hydroxy-4-(3-isoxazolylamino)-1-(1-methylethyl)-4-oxobutyl]-N-methyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



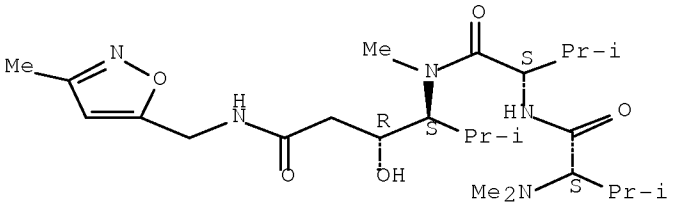
RN 176769-06-5 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[2-hydroxy-1-(1-methylethyl)-4-[(5-methyl-1,3,4-thiadiazol-2-yl)amino]-4-oxobutyl]-N-methyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



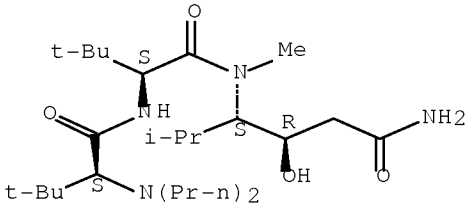
RN 176769-13-4 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-valyl-N-[2-hydroxy-1-(1-methylethyl)-4-[[(3-methyl-5-isoxazolyl)methyl]amino]-4-oxobutyl]-N-methyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



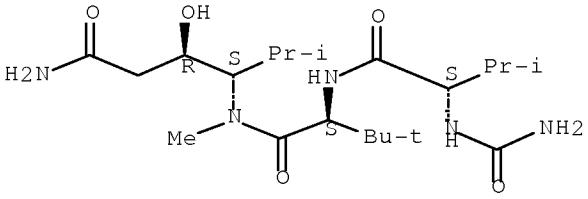
RN 176769-36-1 HCAPLUS
CN L-Valinamide, 3-methyl-N,N-dipropyl-L-valyl-N-[4-amino-2-hydroxy-1-(1-methylethyl)-4-oxobutyl]-N,3-dimethyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



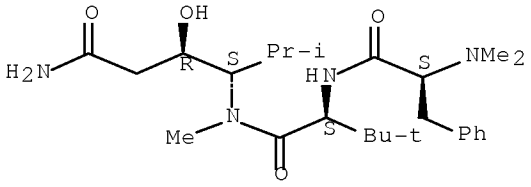
RN 176769-37-2 HCAPLUS
CN L-Valinamide, N-(aminocarbonyl)-L-valyl-N-[4-amino-2-hydroxy-1-(1-methylethyl)-4-oxobutyl]-N,3-dimethyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



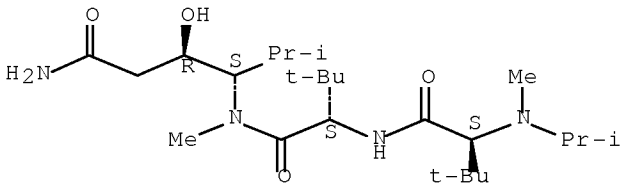
RN 176769-38-3 HCAPLUS
CN L-Valinamide, N,N-dimethyl-L-phenylalanyl-N-[4-amino-2-hydroxy-1-(1-methylethyl)-4-oxobutyl]-N,3-dimethyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 176769-39-4 HCAPLUS
CN L-Valinamide, N,3-dimethyl-N-(1-methylethyl)-L-valyl-N-[4-amino-2-hydroxy-1-(1-methylethyl)-4-oxobutyl]-N,3-dimethyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K038-07
ICS A61K038-06
INCL 514017000
CC 1-6 (Pharmacology)
Section cross-reference(s): 34
IT Neoplasm inhibitors
Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as antitumor agents)
IT 160453-09-8P 160453-10-1P 176768-08-4P 176768-09-5P 176768-10-8P
176768-11-9P 176768-12-0P 176768-13-1P 176768-14-2P 176768-15-3P
176768-16-4P 176768-17-5P 176768-18-6P 176768-19-7P 176768-20-0P
176768-21-1P 176768-22-2P 176768-23-3P 176768-24-4P 176768-25-5P
176768-26-6P 176768-27-7P 176768-28-8P 176768-29-9P 176768-30-2P
176768-31-3P 176768-32-4P 176768-33-5P 176768-34-6P 176768-35-7P
176768-36-8P 176768-37-9P 176768-38-0P 176768-39-1P 176768-40-4P
176768-41-5P 176768-42-6P 176768-43-7P 176768-44-8P 176768-45-9P
176768-46-0P 176768-47-1P 176768-48-2P 176768-49-3P
176768-50-6P 176768-51-7P 176768-52-8P 176768-53-9P 176768-54-0P
176768-55-1P 176768-56-2P 176768-57-3P 176768-58-4P
176768-59-5P 176768-60-8P 176768-61-9P 176768-62-0P 176768-63-1P
176768-64-2P 176768-65-3P 176768-66-4P 176768-67-5P
176768-68-6P 176768-69-7P 176768-70-0P 176768-71-1P 176768-72-2P
176768-73-3P 176768-74-4P 176768-75-5P 176768-76-6P 176768-77-7P
176768-78-8P 176768-79-9P 176768-80-2P 176768-81-3P 176768-82-4P
176768-83-5P 176768-84-6P 176768-85-7P 176768-86-8P 176768-87-9P
176768-88-0P 176768-89-1P 176768-90-4P 176768-91-5P 176768-92-6P
176768-93-7P 176768-94-8P 176768-95-9P 176768-96-0P
176768-97-1P 176768-98-2P 176768-99-3P 176769-00-9P 176769-01-0P
176769-02-1P 176769-03-2P 176769-04-3P 176769-05-4P

176769-06-5P 176769-07-6P 176769-08-7P 176769-09-8P
176769-10-1P 176769-11-2P 176769-12-3P 176769-13-4P
176769-14-5P 176769-15-6P 176769-16-7P 176769-17-8P 176769-18-9P
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176769-24-7P 176769-25-8P 176769-26-9P 176769-27-0P 176769-28-1P
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176769-34-9P 176769-35-0P 176769-36-1P 176769-37-2P
176769-38-3P 176769-39-4P 176769-40-7P 176769-41-8P
176769-42-9P 176769-43-0P 176769-44-1P 176769-45-2P 176769-46-3P
176769-47-4P 176769-48-5P 176769-49-6P 176799-49-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as antitumor agents)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 53 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:435632 HCAPLUS Full-text
DOCUMENT NUMBER: 122:214533
ORIGINAL REFERENCE NO.: 122:39242h,39243a
TITLE: Preparation of tetrapeptide amide derivatives, dolastatin 10 analogs, as anticancer and antitumor agents
INVENTOR(S): Sakakibara, Kyoichi; Gondo, Masaaki; Myazaki, Koichi
PATENT ASSIGNEE(S): Teikoku Hormone Mfg Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06234790	A	19940823	JP 1993-43323	19930209
PRIORITY APPLN. INFO.:			JP 1993-43323	19930209

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Tetrapeptides (I; R1 = R2 = R3 = iso-Pr; R1 = H, R2 = iso-Pr, R3 = sec-Bu; R1 = iso-Bu, R2 = R3 = sec-Bu; R1 = me, R2 = iso-Pr, R3 = sec-Bu), having cell proliferation-inhibiting and/or antineoplastic activity more potent than that of dolastatin 10 (no data), are prepared Thus, Z-Val-OH was treated with carbonyldiimidazole in THF and reacted under ice-cooling for 6 h with a reaction mixture obtained by heating malonic acid monomethyl ester K salt with MgCl2 in THF at 55° for 6 h to give valine derivative (II). II was reduced by NaBH4 in MeOH to an alc. (III; R = H, R1 = Z, R2 = Me) and methylated by MeI and Ag2O in DMF to give III (R = R2 = Me, R1 = Z) which was converted into tripeptide derivative III (R = Me, R1 = Q, R2 = tert-butyl). The latter tripeptide derivative was deprotected with CF3CO2H in CH2Cl2 and condensed with amide (IV.HCl) (preparation given) by using (EtO)2P(O)CN and Et3N in DMF to give title compound (V). A total of 4 I were prepared
IT 161712-06-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for preparation of tetrapeptide amide derivs. (dolastatin 10 analogs) as anticancer and antitumor agents)

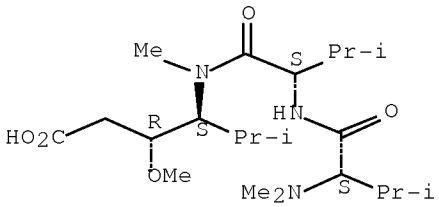
RN 161712-06-7 HCAPLUS

CN L-Valinamide, N,N-dimethyl-L-valyl-N-[3-carboxy-2-methoxy-1-(1-methylethyl)propyl]-N-methyl-, [R-(R*,S*)]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

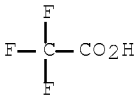
CRN 161712-05-6
CMF C21 H41 N3 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IC ICM C07K005-06
ICA A61K037-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT Neoplasm inhibitors
(preparation of tetrapeptide amide derivs. (dolastatin 10 analogs) as anticancer and antitumor agents)

IT 120205-50-7P 120205-52-9P 120205-58-5P 147778-59-4P 149606-39-3P
149606-41-7P 149606-47-3P 149606-52-0P 149606-56-4P 149606-61-1P
149606-64-4P 149606-68-8P 149606-70-2P 149606-89-3P 149632-87-1P
149632-88-2P 149664-79-9P 161712-03-4P 161712-04-5P
161712-06-7P 161814-03-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for preparation of tetrapeptide amide derivs. (dolastatin 10 analogs) as anticancer and antitumor agents)

L76 ANSWER 54 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:474291 HCAPLUS Full-text

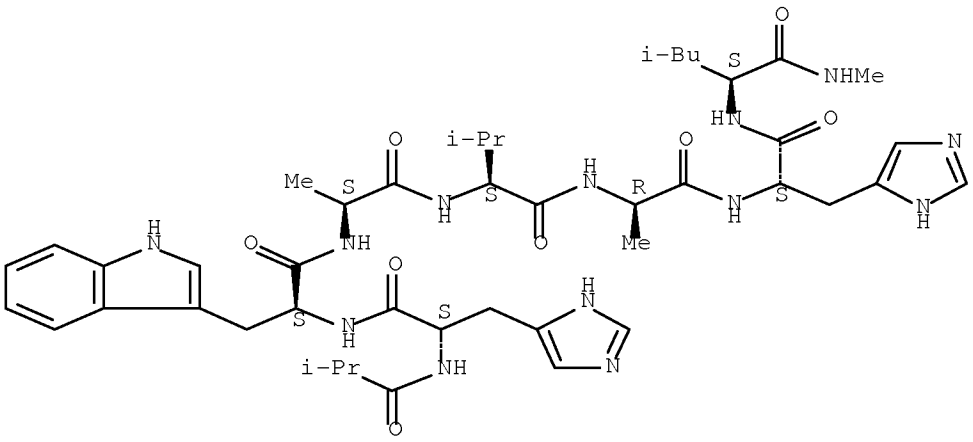
DOCUMENT NUMBER: 121:74291
ORIGINAL REFERENCE NO.: 121:13118h,13119a
TITLE: Characterization of a bombesin/gastrin-releasing peptide receptor on a human gastric-cancer cell line
AUTHOR(S): Preston, Shaun R.; Woodhouse, Linda F.; Gokhale, Jay; Miller, Glenn V.; Primrose, John N.
CORPORATE SOURCE: Academic Unit Surgery, St. James's University Hospital, Leeds, LS9 7TF, UK
SOURCE: International Journal of Cancer (1994), 57(5), 734-41
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study examined the expression of receptors of the bombesin (BBS) family in human gastric-cancer cell lines. Of 5 cell lines screened, only one, St42, demonstrated specific binding sites for 125I-Tyr4-BBS, which have been further characterized. This binding was saturable, and temperature- and time-dependent. Scatchard anal. of displacement data performed at 37° revealed 2 binding sites: a high-affinity, low-capacity site (KD = 0.13 nM, Bmax = 1500 sites/cell) and a lower-affinity, higher-capacity site (KD = 11 nM, Bmax = 35,000 sites/cell); the latter was lost when internalization of peptide was prevented, suggesting that it may be an artifact. Displacement assays with gastrin-releasing peptide (GRP) and neuromedin B (NMB) revealed that the receptor was of the GRP-preferring sub-type (GRP IC50 = 0.35 nM; NMB IC50 = 112 nM). Co-valent crosslinking of 125I-Tyr4-BBS to the receptor demonstrated the presence of a single band corresponding to a mol. weight of 37 to 44 kDa on SDS-PAGE, similar to that of the cloned GRP receptor protein core. G-protein linkage of this receptor was demonstrated by selective inhibition of 125I-Tyr4-BBS binding by guanosine nucleotides. The binding of BBS to the receptor resulted in a rise in intracellular calcium. Three of four structurally distinct BBS antagonists bound to the receptor with high affinity, but [DPhe12, Leu14]-bombesin did not cause any displacement of 125I-Tyr4-BBS even at 10 mM. The functional significance of GRP receptors on human gastric-cancer cells is as yet unknown, but further studies may determine whether such receptors have importance in the therapy of gastric cancer.

IT 124001-41-8, ICI 216140
RL: BIOL (Biological study)
(gastrin-releasing peptide receptor affinity for, of human gastric cancer cells)

RN 124001-41-8 HCAPLUS
CN 3-9-Neuromedin C (swine spinal cord), N-(2-methyl-1-oxopropyl)-7-D-alanine-9-(N-methyl-L-leucinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 2-6 (Mammalian Hormones)
ST bombesin receptor stomach cancer; gastrin releasing peptide receptor stomach cancer
IT Signal transduction, biological
(by gastrin-releasing peptide receptors, in gastric cancer cells of human, calcium in mediation of)
IT G proteins (guanine nucleotide-binding proteins)
RL: BIOL (Biological study)
(gastrin-releasing peptide coupled to, of gastric cancer cells of human)
IT Stomach, neoplasm
(gastrin-releasing peptide receptors of, of human, characterization of)
IT Receptors
RL: PROC (Process)
(gastrin-releasing peptide, of stomach cancer cells, of human, characterization of)
IT 108437-88-3, [D-Phe12,Leu14]bombesin 124001-41-8, ICI 216140
124176-04-1, [D-Phe6,Des-Met14]bombesin(6-13)ethylamide 138147-78-1, RC-3095
RL: BIOL (Biological study)
(gastrin-releasing peptide receptor affinity for, of human gastric cancer cells)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(of stomach cancer cells, gastrin-releasing peptide receptor signal transduction mediation by)
IT 80043-53-4, Gastrin-releasing peptide
RL: BIOL (Biological study)
(receptors for, of gastric cancer cells of human, characterization of)

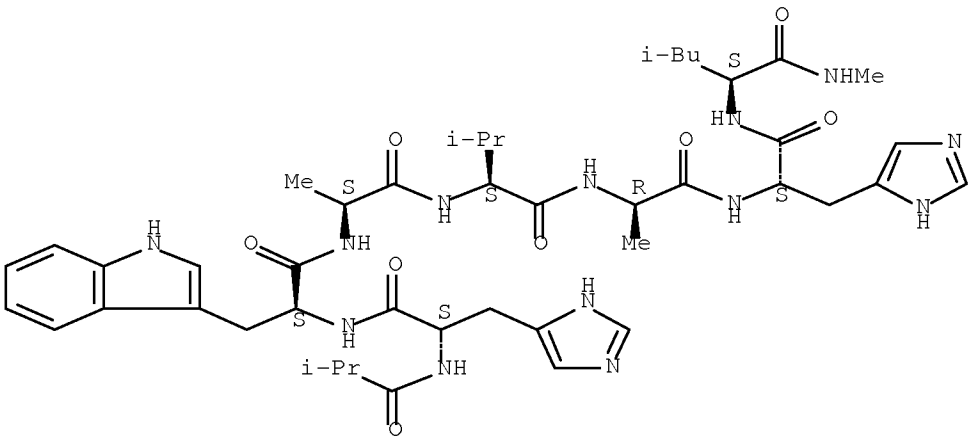
L76 ANSWER 55 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:96458 HCAPLUS Full-text
DOCUMENT NUMBER: 120:96458
ORIGINAL REFERENCE NO.: 120:16971a,16974a
TITLE: Two bombesin analogs discriminate between neuromedin B- and bombesin-induced calcium flux in a lung cancer cell line
AUTHOR(S): Ryan, R. R.; Daniel, J. L.; Cowan, A.
CORPORATE SOURCE: Sch. Med., Temple Univ., Philadelphia, PA, 19140, USA
SOURCE: Peptides (New York, NY, United States) (1993), 14(6),

1231-5
CODEN: PPTDD5; ISSN: 0196-9781
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examined the profile of two bombesin (BN) antagonists, (CH3)2CHCO-His-Trp-Ala-Val-D-Ala-His-Leu-NHCH3 (ICI 216140) and [D-Phe6,des-Met14]BN(6-14)ethylamide (DPDM-BN EA), against neuromedin B-induced Ca2+ mobilization in the small cell lung cancer (SCLC) line NCI-H345. Neuromedin B (NMB), a BN-like peptide sharing sequence homol. with ranatensin, elicited a concentration-dependent Ca2+ release (in part) from intracellular stores. Sequential addition of NMB attenuated Ca2+ mobilization. Desensitization occurred between BN and NMB; depletion of intracellular Ca2+ is a likely mechanism because thapsigargin stimulated Ca2+ release after a maximally desensitizing dose of NMB. ICI 216140 and DPDM-BN EA competitively inhibited BN-induced Ca2+ transients. In contrast, these compds. antagonized NMB-stimulated Ca2+ transients in a noncompetitive manner. The pharmacol. profiles obtained support receptor heterogeneity for BN-like peptides on this SCLC line, underscoring the need for thorough examination of dose-response relationships when investigating effects of BN analogs on intact cells.

IT 124001-41-8, ICI 216140
RL: BIOL (Biological study)
(calcium transport inhibition by, in lung neoplasm after bombesin and neuromedin B stimulation)
RN 124001-41-8 HCAPLUS
CN 3-9-Neuromedin C (swine spinal cord), N-(2-methyl-1-oxopropyl)-7-D-alanine-9-(N-methyl-L-leucinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 2-6 (Mammalian Hormones)
ST calcium flux bombesin neuromedin B; bombesin calcium flux lung cancer; neuromedin B calcium flux lung; lung cancer calcium flux peptide
IT Lung, neoplasm
(calcium transport by, bombesin and neuromedin B effect on)
IT Biological transport
(of calcium, by lung neoplasm, bombesin and neuromedin B effect on)
IT 31362-50-2, Bombesin 102577-19-5, Neuromedin B
RL: BIOL (Biological study)

(calcium transport in response to, in lung neoplasm, bombesin analogs effect on)
IT 124001-41-8, ICI 216140 124199-90-2
RL: BIOL (Biological study)
(calcium transport inhibition by, in lung neoplasm after bombesin and neuromedin B stimulation)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(transport of, by lung neoplasm, bombesin and neuromedin B effect on)

L76 ANSWER 56 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:27456 HCAPLUS Full-text
DOCUMENT NUMBER: 118:27456
ORIGINAL REFERENCE NO.: 118:4973a,4976a
TITLE: Covalent lipid-drug conjugates for drug targeting
INVENTOR(S): Yatvin, Milton B.; Parks, David W.; McClard, Ronald W.; Stowell, Michael H. B.; Witte, John F.
PATENT ASSIGNEE(S): State of Oregon, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5149794	A	19920922	US 1990-607982	19901101
US 5256641	A	19931026	US 1992-911209	19920709
US 5543389	A	19960806	US 1993-142771	19931026
US 5543390	A	19960806	US 1994-246941	19940519
US 5543391	A	19960806	US 1995-441770	19950516
US 5965519	A	19991012	US 1996-685152	19960723
US 5840674	A	19981124	US 1996-691891	19960801
US 5827819	A	19981027	US 1996-735977	19961025
US 6024977	A	20000215	US 1997-923015	19970903
US 6063759	A	20000516	US 1998-60011	19980414
US 6387876	B1	20020514	US 1999-415640	19991012
US 6436437	B1	20020820	US 2000-503892	20000215
US 6339060	B1	20020115	US 2000-573497	20000516
US 20040087482	A1	20040506	US 2002-50271	20020115
US 6858582	B2	20050222		
US 20020173498	A1	20021121	US 2002-144516	20020513

PRIORITY APPLN. INFO.:		
US 1990-607982	A2	19901101
US 1992-911209	A2	19920709
US 1993-142771	A2	19931026
US 1994-246941	A3	19940519
US 1995-441770	A1	19950516
US 1996-685152	A2	19960723
US 1996-691891	A1	19960801
US 1996-735977	A3	19961025
US 1997-923015	A3	19970903
US 1998-60011	A1	19980414
US 1999-415640	A3	19991012
US 2000-573497	A3	20000516

AB A method of drug targeting comprises covalently binding a drug to a lipid carrier. This composition has the ability to both enhance the rate at which an antineoplastic or antiviral drug crosses the plasma membrane, and to direct the drug within the cell to specific organelles. The versatility of these

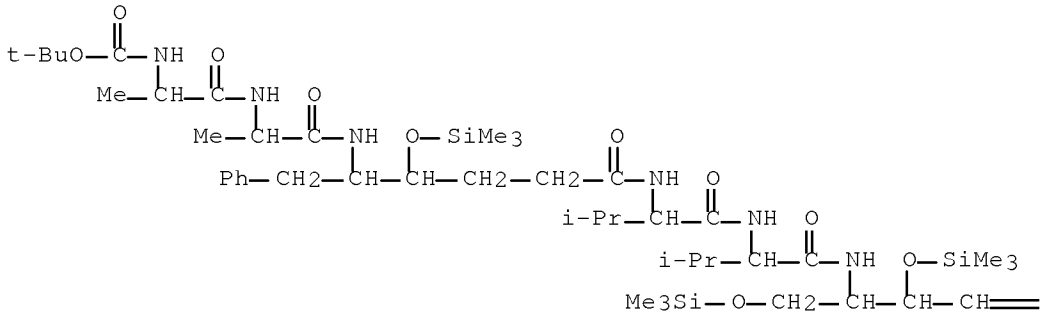
conjugates may be further enhanced by including a spacer group between the drug and the lipid which may act to modulate drug release at the target site. The lipids are sphingosine, ceremide, phosphatidylcholines, etc. Sphingosine was reacted with 5-fluorodeoxyuridine, in the presence of dichlorophenyl phosphate (Baer, 1955) to give a conjugate.

IT 145069-69-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

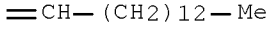
RN 145069-69-8 HCAPLUS

CN L-Valinamide, N-[5-[[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-alanyl]amino]-1-oxo-6-phenyl-4-[(trimethylsilyl)oxy]hexyl]-L-valyl-N-[2-[(trimethylsilyl)oxy]-1-[[(trimethylsilyl)oxy]methyl]-3-heptadecenyl]-, [1[S-(R*,R*)],2[R-[R*,S*-(E)]]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC ICM C07H017-00
ICS A61K037-22; A61K031-70

INCL 536029000

CC 63-5 (Pharmaceuticals)

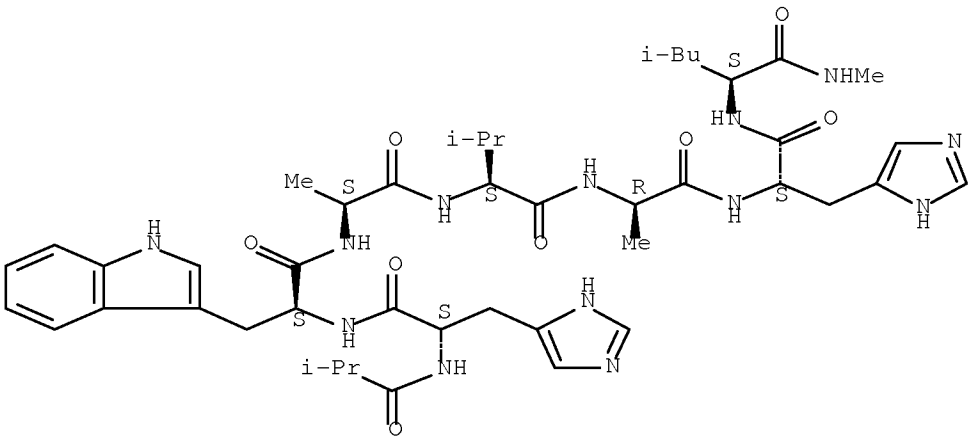
IT Neoplasm inhibitors
Virucides and Virustats
(conjugates with polar lipid carriers, for targeted delivery and facilitated release)

IT Phosphatidic acids

Phosphatidylglycerols
RL: BIOL (Biological study)
(reaction products, with neoplasm inhibitors and virucides, targeted drug delivery and facilitated drug release by)
IT Lipids, compounds
RL: BIOL (Biological study)
(conjugates, with neoplasm inhibitors and virucides, for targeted delivery and facilitated release)
IT Phosphatidylcholines, compounds
Phosphatidylethanolamines
RL: BIOL (Biological study)
(reaction products, with neoplasm inhibitors and virucides, targeted drug delivery and facilitated drug release by)
IT 145069-69-8P 145069-73-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)
IT 145069-76-7P
RL: PREP (Preparation)
(preparation of, as neoplasm inhibitor for targeting)
IT 123-78-4D, Sphingosine, conjugates with neoplasm inhibitors and virucides 2304-81-6D, conjugates with neoplasm inhibitors and virucides
RL: BIOL (Biological study)
(targeted drug delivery and facilitated drug release by)

L76 ANSWER 57 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:241002 HCAPLUS Full-text
DOCUMENT NUMBER: 114:241002
ORIGINAL REFERENCE NO.: 114:40505a,40508a
TITLE: ICI 216140 and other potent in vivo antagonist analogs of bombesin/gastrin-releasing peptide
AUTHOR(S): Camble, R.; Cotton, R.; Dutta, A. S.; Garner, A.; Hayward, C. F.; Moore, V. E.; Scholes, P. B.
CORPORATE SOURCE: ICI Pharm., Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 174-6. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.
CODEN: 56XTA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A report from a symposium on the preparation and activity of bombesin and gastrin-releasing peptide truncated and side chain deletion analogs. Heptapeptide derivs. RCO-His-Trp-Ala-Val-D-Ala-His-R1 [R = Me2CH, R1 = Leu-NHMe (ICI 216140); R = Et, R1 = MeLeu-OMe (ICI 216167)] were potent inhibitors of amylase secretion and displayed prolonged duration of action.
IT 124001-41-8P, ICI 216140
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bombesin antagonistic activity of)
RN 124001-41-8 HCAPLUS
CN 3-9-Neuromedin C (swine spinal cord), N-(2-methyl-1-oxopropyl)-7-D-alanine-9-(N-methyl-L-leucinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 2-6 (Mammalian Hormones)
ST ICI 216140 bombesin antagonist symposium; gastrin releasing peptide antagonist ICI 216167; neoplasm inhibitor bombesin analog symposium
IT Neoplasm inhibitors
(bombesin and gastrin-releasing peptide truncated and side chain deletion analogs)
IT 31362-50-2DP, Bombesin, truncated and side chain deletion analogs
80043-53-4DP, Gastrin-releasing peptide, truncated and side chain deletion analogs 124000-48-2P, ICI 216167 124001-41-8P, ICI 216140
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bombesin antagonistic activity of)

L76 ANSWER 58 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1990:7930 HCAPLUS Full-text
DOCUMENT NUMBER: 112:7930
ORIGINAL REFERENCE NO.: 112:1558h,1559a
TITLE: Preparation of peptides as antagonists against bombesin or bombesin-like peptides
INVENTOR(S): Camble, Roger; Cotton, Ronald; Dutta, Anand Swaroop; Hayward, Christopher Frederick
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 315367	A2	19890510	EP 1988-310094	19881027
EP 315367	A3	19901128		
EP 315367	B1	19940406		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8807699	A	19890628	ZA 1988-7699	19881014
AU 8824142	A	19890504	AU 1988-24142	19881021
AU 618029	B2	19911212		
US 5068222	A	19911126	US 1988-265566	19881101
DK 8806109	A	19890503	DK 1988-6109	19881102
JP 01151599	A	19890614	JP 1988-276355	19881102

PRIORITY APPLN. INFO.: GB 1987-25598 A 19871102
GB 1988-3478 A 19880215
GB 1988-13355 A 19880606

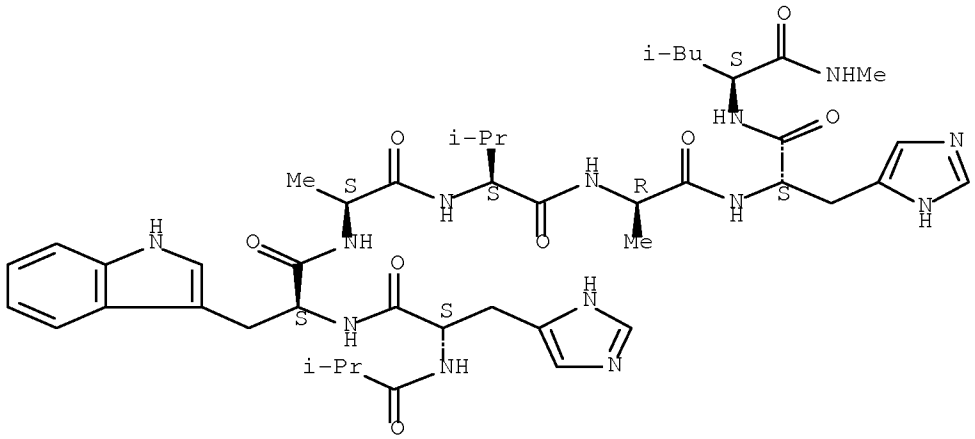
AB R1-A1-A2-A3-A4-A5-A6-A7-A8-A9-Q [I; R1 = H, alkylcycloalkoxycarbonyl, etc.; A1 = bond, Gly, Arg, D-Arg, Lys, Phe, etc.; A2 = bond, Gly, Pro, Asn; A3 = bond, Lys, Lys(Z), etc.; A4 = His, MeHis, EtHis, etc.; A5 = Trp, MeTrp, Lys, Leu, etc.; A6 = Ala, MeAla, Gly, etc.; A7 = Val, MeVal, Leu, etc.; A8 = Gly, Ala, D-Ser, A9 = His, Val, Leu, Ala, etc.; Q = (substituted) amino acid residue] and their pharmaceutically acceptable salts, useful as antagonists against bombesin-like peptides and for treatment of cancer (no data), are prepared Z-Arg-Pro-Lys(Z)-His-Trp-Ala-Val-D-Ala-His-Leu-OMe (Z = PhCH2O2C) was prepared via solid-phase synthesis starting from BOC-Leu-OH (BOC = Me3CO2C).

IT 124001-41-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as bombesin antagonist)

RN 124001-41-8 HCAPLUS

CN 3-9-Neuromedin C (swine spinal cord), N-(2-methyl-1-oxopropyl)-7-D-alanine-9-(N-methyl-L-leucinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K007-00
ICS A61K037-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63

IT Neoplasm inhibitors
(bombesin antagonistic peptides)

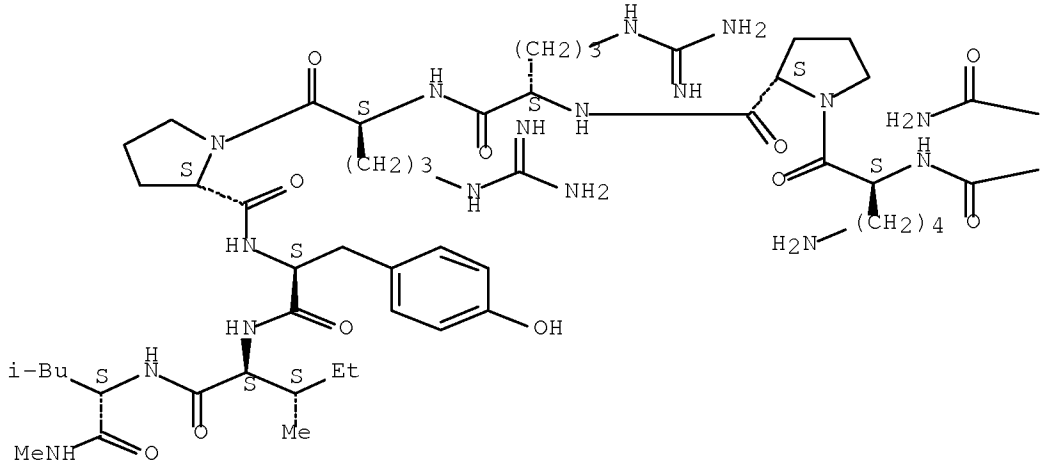
IT 123983-14-2P 124000-13-1P 124000-14-2P 124000-15-3P 124000-16-4P
124000-17-5P 124000-18-6P 124000-19-7P 124000-20-0P 124000-21-1P
124000-22-2P 124000-23-3P 124000-24-4P 124000-25-5P 124000-26-6P
124000-27-7P 124000-28-8P 124000-29-9P 124000-30-2P 124000-31-3P
124000-32-4P 124000-33-5P 124000-34-6P 124000-35-7P 124000-36-8P
124000-37-9P 124000-38-0P 124000-39-1P 124000-40-4P 124000-41-5P
124000-42-6P 124000-43-7P 124000-44-8P 124000-45-9P 124000-46-0P
124000-47-1P 124000-48-2P 124000-49-3P 124000-50-6P 124000-51-7P
124000-52-8P 124000-53-9P 124000-54-0P 124000-55-1P 124000-56-2P
124000-57-3P 124000-58-4P 124000-59-5P 124000-60-8P 124000-61-9P
124000-62-0P 124000-63-1P 124000-64-2P 124000-65-3P 124000-66-4P
124000-67-5P 124000-68-6P 124000-69-7P 124000-70-0P 124000-71-1P
124000-72-2P 124000-73-3P 124000-74-4P 124000-75-5P 124000-76-6P

124000-77-7P 124000-78-8P 124000-79-9P 124000-80-2P 124000-81-3P
124000-82-4P 124000-83-5P 124000-84-6P 124000-85-7P 124000-86-8P
124000-87-9P 124000-88-0P 124000-89-1P 124000-90-4P 124000-91-5P
124000-92-6P 124000-93-7P 124000-94-8P 124000-95-9P 124000-96-0P
124000-97-1P 124000-98-2P 124000-99-3P 124001-00-9P 124001-01-0P
124001-02-1P 124001-03-2P 124001-04-3P 124001-05-4P 124001-06-5P
124001-07-6P 124001-08-7P 124001-09-8P 124001-10-1P 124001-11-2P
124001-12-3P 124001-13-4P 124001-14-5P 124001-15-6P 124001-16-7P
124001-17-8P 124001-18-9P 124001-19-0P 124001-20-3P 124001-21-4P
124001-22-5P 124001-23-6P 124001-24-7P 124001-25-8P 124001-26-9P
124001-27-0P 124001-28-1P 124001-29-2P 124001-30-5P 124001-31-6P
124001-32-7P 124001-33-8P 124001-34-9P 124001-35-0P 124001-36-1P
124001-37-2P 124001-38-3P 124001-39-4P 124001-40-7P
124001-41-8P 124001-42-9P 124001-43-0P 124001-44-1P
124001-45-2P 124001-46-3P 124001-47-4P 124001-48-5P 124001-49-6P
124001-50-9P 124001-52-1P 124020-52-6P 124027-11-8P 124027-12-9P
124027-13-0P 124027-14-1P 124027-15-2P 124027-16-3P 124096-04-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as bombesin antagonist)

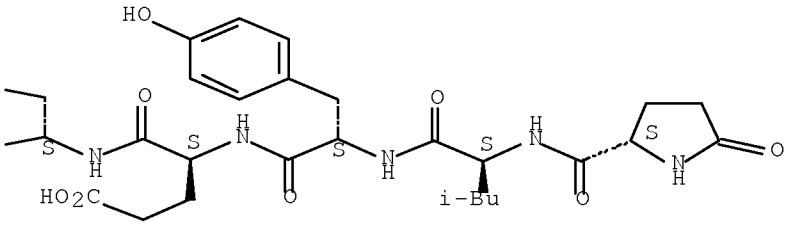
L76 ANSWER 59 OF 59 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:123273 HCAPLUS Full-text
DOCUMENT NUMBER: 104:123273
ORIGINAL REFERENCE NO.: 104:19323a,19326a
TITLE: Neurotensin and its analogs - correlation of specific binding with stimulation of cyclic GMP formation in neuroblastoma clone N1E-115
AUTHOR(S): Gilbert, Judith A.; Moses, C. Jill; Pfenning, Michael A.; Richelson, Elliott
CORPORATE SOURCE: Dep. Psychiatry, Mayo Clin. Mayo Found., Rochester, MN, 55905, USA
SOURCE: Biochemical Pharmacology (1986), 35(3), 391-7
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The receptors which mediate neurotensin [39379-15-2]-stimulated intracellular cyclic GMP [7665-99-8] formation in murine neuroblastoma clone N1E-115 (Gilbert J. A.; Richelson E. 1984) were further characterized. The binding of [3H]neurotensin to intact N1E-115 cells at 0° displayed specificity, saturability, reversibility, and tissue linearity. A single class of neurotensin receptors was demonstrated with an apparent dissociation constant (KD) of 9-11 nM and a maximum binding capacity of 180-250 fmoles/106 cells, determined by the type of serum employed in the cellular culture medium. A number of neurotensin analogs and fragments were compared for their ability to inhibit [3H]neurotensin binding and stimulate intracellular cyclic GMP formation with intact N1E-115 cells. A direct correlation exists between the KD and concentration for half maximal stimulation for each peptide. The carboxyl-terminal portion of neurotensin was responsible for the binding and biochem. activities of this peptide with clone N1E-115. Neurotensin(8-13) [60482-95-3] was 50-fold more potent than native neurotensin in stimulating intracellular cyclic GMP formation and had an 18-fold higher affinity for the neurotensin receptor on this neuronal cell type.
IT 64240-09-1
RL: BIOL (Biological study)
(cyclic GMP formation stimulation by, in neuroblastoma clone, mol. structure and specific binding in relation to)
RN 64240-09-1 HCAPLUS
CN Neurotensin (cattle), 13-(N-methyl-L-leucinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CC 2-2 (Mammalian Hormones)

IT Nerve, neoplasm
(neuroblastoma, cGMP accumulation and receptor binding of neurotensin and analogs in, analog mol. structure in relation to)

IT 39379-15-2 39379-15-2D, analogs 60482-95-3 60482-96-4 61445-54-3
63524-00-5 63770-61-6 64088-60-4 64088-61-5 64088-62-6
64088-65-9 64088-66-0 64240-09-1 73634-68-1 74032-89-6
80887-44-1 87620-09-5
RL: BIOL (Biological study)
(cyclic GMP formation stimulation by, in neuroblastoma clone, mol. structure and specific binding in relation to)

******* SEARCH HISTORY *******

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=> d his nofi

     (FILE 'HOME' ENTERED AT 13:40:22 ON 09 MAR 2009)

     FILE 'REGISTRY' ENTERED AT 13:40:41 ON 09 MAR 2009
L1          336 SEA ABB=ON  PLU=ON  TETRAMETHYL (L) TYROSYL?
L2           26 SEA ABB=ON  PLU=ON  L1 (L) VALINAMIDE
L3           21 SEA ABB=ON  PLU=ON  L2 (L) BUTENYL
L4           12 SEA ABB=ON  PLU=ON  L3 (L) CARBOXY
L5            0 SEA ABB=ON  PLU=ON  L4 (L) ISOPROPYL
L6            8 SEA ABB=ON  PLU=ON  L4 (L) DIMETHYL
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 13:43:21 ON 09 MAR 2009

     FILE 'REGISTRY' ENTERED AT 13:49:28 ON 09 MAR 2009
L7           86 SEA ABB=ON  PLU=ON  C28H45N3O5/MF
L8            6 SEA ABB=ON  PLU=ON  L7 AND VALINAMIDE
L9            3 SEA ABB=ON  PLU=ON  L8 AND TYROSYL
L10           1 SEA ABB=ON  PLU=ON  L9 AND CARBOXY
                D IDE
L11           1 SEA ABB=ON  PLU=ON  676633-18-4/RN
L12           1 SEA ABB=ON  PLU=ON  L10 OR L11

     FILE 'STNGUIDE' ENTERED AT 13:52:43 ON 09 MAR 2009

     FILE 'HCAPLUS' ENTERED AT 13:56:34 ON 09 MAR 2009
L13           1 SEA ABB=ON  PLU=ON  L12
L14           1 SEA ABB=ON  PLU=ON  US20040121965/PN
                SEL RN

     FILE 'REGISTRY' ENTERED AT 13:57:17 ON 09 MAR 2009
L15         566 SEA ABB=ON  PLU=ON  (100-66-3/BI OR 100564-78-1/BI OR 104-87-0/
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                -1/BI OR 128437-74-1/BI OR 13139-15-6/BI OR 13734-34-4/BI OR
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                -2/BI OR 676627-
L16           286 SEA ABB=ON  PLU=ON  L15 AND VALINAMIDE
L17           283 SEA ABB=ON  PLU=ON  L15 AND "L-VALINAMIDE"
L18           248 SEA ABB=ON  PLU=ON  L15 AND "PHENYLALANYL"
L19            41 SEA ABB=ON  PLU=ON  L15 AND "VALYL"
L20           229 SEA ABB=ON  PLU=ON  L15 AND CARBOXY
L21            54 SEA ABB=ON  PLU=ON  L15 AND TETRAMETHYL?
L22           410 SEA ABB=ON  PLU=ON  L15 AND DIMETHYL?
L23           248 SEA ABB=ON  PLU=ON  L22 AND VALINAMIDE
L24            33 SEA ABB=ON  PLU=ON  L15 AND HEXENOIC ACID
L25            27 SEA ABB=ON  PLU=ON  L16 AND TYROSYL
L26             5 SEA ABB=ON  PLU=ON  L15 AND TYROSINAMIDE
L27            11 SEA ABB=ON  PLU=ON  L15 AND ALLOTHREONINAMIDE
L28             7 SEA ABB=ON  PLU=ON  L15 AND PHENYLALANINAMIDE
L29            12 SEA ABB=ON  PLU=ON  L15 AND LEUCINAMIDE
L30             0 SEA ABB=ON  PLU=ON  L15 AND "HEX-2-ENOIC ACID"
L31             2 SEA ABB=ON  PLU=ON  L15 AND NORVALINAMIDE
L32             0 SEA ABB=ON  PLU=ON  L15 AND HEXENAMIDE
L33            10 SEA ABB=ON  PLU=ON  L15 AND ISOLEUCINAMIDE
L34             4 SEA ABB=ON  PLU=ON  L15 AND PENTENOIC ACID
L35             0 SEA ABB=ON  PLU=ON  L15 AND DIMETHYLHEXANOIC ACID
L36             1 SEA ABB=ON  PLU=ON  L15 AND "L-()A()GLUTAMINE"
                D SCAN
L37           349 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19 OR L20 OR L21)
L38           328 SEA ABB=ON  PLU=ON  (L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
                L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36)
L39           386 SEA ABB=ON  PLU=ON  L37 OR L38

     FILE 'HCAPLUS' ENTERED AT 14:31:56 ON 09 MAR 2009
L40         28511 SEA ABB=ON  PLU=ON  L39
                E CHEMOTHERAPEUTIC AGENTS/CT
                E E3+ALL
                D SC L14
                E OVARIAN CANCER/CT
                E E3+ALL
L41         24618 SEA ABB=ON  PLU=ON  "OVARY, NEOPLASM"/CT
L42         35118 SEA ABB=ON  PLU=ON  (OVARIAN OR OVARY OR OVARIES) (S) (CANCER?
                OR TUMOR? OR TUMOUR? OR NEOPLAS? OR CARCIN?)
L43          2529 SEA ABB=ON  PLU=ON  L40 AND L41
L44          2933 SEA ABB=ON  PLU=ON  L40 AND L42
L45          5205 SEA ABB=ON  PLU=ON  (L41 OR L42) (L) ((CHEMOTHERAP? OR
                ANTI(W)TUMOR# OR ANTITUMOR# OR ANTI(W)TUMOUR# OR ANTI(W)TUMOUR#
                ) (S) AGENT#)
L46          1238 SEA ABB=ON  PLU=ON  L40 AND L45
L47         20157 SEA ABB=ON  PLU=ON  (L41 OR L42) (S) (INHIB? OR ERADICAT? OR
                TREAT# OR TREATMEN# OR TREATING)
L48          4360 SEA ABB=ON  PLU=ON  L45 AND L47
L49          1049 SEA ABB=ON  PLU=ON  L40 AND L48

     FILE 'STNGUIDE' ENTERED AT 15:21:45 ON 09 MAR 2009

     FILE 'REGISTRY' ENTERED AT 15:46:52 ON 09 MAR 2009
L50             0 SEA ABB=ON  PLU=ON  3(W)(DIMETHYL? OR METHYLSUL?) (2W)
                VALINAMIDE
L51          2185 SEA ABB=ON  PLU=ON  3(L)(DIMETHYL?) (L) VALINAMIDE
L52         16609 SEA ABB=ON  PLU=ON  2 (L) ((HEXENO? OR HEXEONATE OR HEP(W)ENOIC
                ) (W) ACID)
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L53           46 SEA ABB=ON  PLU=ON  METHYL? (2W) VALINAMIDE
L54            1 SEA ABB=ON  PLU=ON  METHYL? (2W) ALLOTHREONINAMIDE
L55            0 SEA ABB=ON  PLU=ON  TRIMETHYL(2W) PHENYLALANIMIDE
L56            0 SEA ABB=ON  PLU=ON  ETHYL (2W) VALIMIDE
L57           92 SEA ABB=ON  PLU=ON  (DIMETHYL OR METHYL) (2W) LEUCINAMIDE
L58            0 SEA ABB=ON  PLU=ON  METHYL (2W) NORVALINAMIDE
L59            7 SEA ABB=ON  PLU=ON  METHYL (2W) ISOLEUCINAMIDE
L60            0 SEA ABB=ON  PLU=ON  TRIMETHYL (2W) HEXENAMIDE
L61            4 SEA ABB=ON  PLU=ON  DIMETHYL (2W) HEXENAMIDE
L62           91 SEA ABB=ON  PLU=ON  PHENYL? (2W) PENTENOI?
L63            1 SEA ABB=ON  PLU=ON  METHYL? (2W) NORVALINAMIDE
L64            1 SEA ABB=ON  PLU=ON  TRIMETHYL? (2W) HEXENAMID?
L65            0 SEA ABB=ON  PLU=ON  PHENYL? (2W) (A(W) GLUTAMID?)
L66            0 SEA ABB=ON  PLU=ON  METHASULFAN? (W) BUTYRIC ACID?
L67        19034 SEA ABB=ON  PLU=ON  (L51 OR L52 OR L53 OR L54) OR L57 OR L59
                 OR L61 OR L62 OR (L63 OR L64)
                 SAVE TEMP L67 JEA722COMPS/A

     FILE 'HOME' ENTERED AT 16:00:07 ON 09 MAR 2009

     FILE 'HCAPLUS' ENTERED AT 16:00:19 ON 09 MAR 2009
L68        16296 SEA ABB=ON  PLU=ON  L67
L69          126 SEA ABB=ON  PLU=ON  L68 AND (L41 OR L42)

     FILE 'STNGUIDE' ENTERED AT 16:24:37 ON 09 MAR 2009

     FILE 'REGISTRY' ENTERED AT 16:26:00 ON 09 MAR 2009
L70              STRUCTURE UPLOADED
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Uploading L4.str
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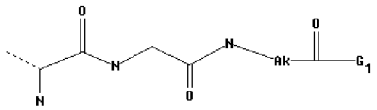

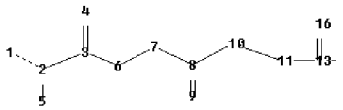


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chain nodes :
2  3  4  6  7  8  9  10  11  13  15  16
ring/chain nodes :
1  5
chain bonds :
1-2  2-3  2-5  3-4  3-6  6-7  7-8  8-9  8-10  10-11  11-13  13-15  13-16
exact/norm bonds :
1-2  2-5  3-4  3-6  6-7  8-9  8-10  10-11  11-13  13-15  13-16
exact bonds :
2-3  7-8


G1:O,S,N
```

```
Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  13:CLASS  15:CLASS  16:CLASS
Element Count :
Node 11: Limited
    C,C1-6




L71          15 SEA SUB=L67 SSS SAM L70
L72         395 SEA SUB=L67 SSS FUL L70
                SAVE TEMP L72 JEA722REGL3/A

     FILE 'HCAPLUS' ENTERED AT 16:29:04 ON 09 MAR 2009
L73         276 SEA ABB=ON  PLU=ON  L72
L74           1 SEA ABB=ON  PLU=ON  L73 AND (L41 OR L42)
                D SCAN TI HIT
L75          60 SEA ABB=ON  PLU=ON  L73 AND (CANCER? OR NEOPLAS? OR TUMOR? OR
                TUMOUR? OR CARCIN?)
L76          59 SEA ABB=ON  PLU=ON  L75 NOT L74

     FILE 'STNGUIDE' ENTERED AT 16:35:25 ON 09 MAR 2009

     FILE 'REGISTRY' ENTERED AT 16:36:45 ON 09 MAR 2009
                D IDE L12

     FILE 'STNGUIDE' ENTERED AT 16:36:46 ON 09 MAR 2009
                D QUE L13

     FILE 'HCAPLUS' ENTERED AT 16:37:07 ON 09 MAR 2009
                D L13 IBIB ABS HITSTR HITIND

     FILE 'STNGUIDE' ENTERED AT 16:37:08 ON 09 MAR 2009
                D QUE L74

     FILE 'HCAPLUS' ENTERED AT 16:38:13 ON 09 MAR 2009
                D L74 1 IBIB ABS HITSTR HITIND

     FILE 'STNGUIDE' ENTERED AT 16:38:15 ON 09 MAR 2009
                D QUE L76

     FILE 'HCAPLUS' ENTERED AT 16:40:03 ON 09 MAR 2009
                D L76 1-59 IBIB ABS HITSTR HITIND

     FILE 'STNGUIDE' ENTERED AT 16:40:42 ON 09 MAR 2009
```